# *AN IN VITRO* STUDY OF *RICINUS COMMUNIS* AND *EUCLEA DIVINORUM* EXTRACTS ON ISOLATED RABBIT UTERUS.

A thesis submitted in partial fulfillment for the award of Master of Science degree of the University of Nairobi. (Reproductive biology)

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## DECLARATION

I hereby declare that this thesis is my original work and has not been presented for a degree in any other University.

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# DEDICATION

To my sons Tevin and Matthew for their love, patience and support,

To my husband, E. Kong'ani for believing in me.

To almighty God for making it possible.

ACKNOWLEDGEMENT

Special thanks to my supervisors Dr. Jemimah Oduma and Professor Titus Kanui for availing their endless support, guidance and encouragement throughout the course of this work. I would also like to thank the 'Deans Committee University of Nairobi' for funding the project.

I wish to extend my heartfelt gratitude to all members of staff, Department of Veterinary Anatomy and Physiology who were very helpful during the course of the study. J. Mugweru, M. Kagina, P. Irungu, S. Kamonde, G. Gikonyo , R. Githinji and D. Kwoba for their support.

To Dr. D.K Kariuki and Mr. Mwangi who supported me with the ethanol and chloroform extraction of both plants.

I am indebted to the Traditional Birth Attendants in Kathiani and Kyevaluki sub locations of Machakos district for sharing their knowledge and time. I am grateful to Nyongesa, Waweru and Githinji for their input, advice and encouragement. To my friends Vivian, Wambugu, Musembi, Dullu and Ochwang'i for precious moments.

Finally to my husband and sons for their sacrifice, support and encouragement during the course of the study.

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| | |
|---|---|
| AED | Aqueous *Euclea divinorum* |
| ARC | Aqueous *Ricinus communis* |
| CED | Chloroform *Euclea divinorum* |
| CRC | Chloroform *Ricinus communis* |
| DMSO | Dimethyl Sulphoxide |
| EED | Ethanol *Euclea divinorum* |
| ERC | Ethanol *Ricinus communis* |
| hCG | Human Chorionic Gonadotrophin |
| HIV/ AIDS | Human Immuno Virus / Acquired Immuno Deficiency Syndrome |
| MDDP | Machakos District Development Plan |
| MDGs | Millenium Development Goals |
| NN | Non pregnant No hormone |
| NPH | Non pregnant Presence of Hormone |
| NHSSP | National Health Sector Strategic Plan |
| OAU | Organization of African Unity |
| OXT | Oxytocin |
| PGF 2α | Prostaglandin F2α |
| PGE | Prostaglandin E |
| PNH | Pregnant No Hormone |

| | |
|---|---|
| PPH | Pregnant Presence of Hormone |
| PPh | Post Partum Haemorrhage |
| RAB | Retained After Birth |
| RHW | Reproductive Health Worker |
| TBAs | Traditional Birth Attendants |
| WHO | World Health Organization |

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## ABSTRACT

Gestation period is sensitive, delicate and prone to several disruptions, the commonest being spontaneous abortions, hypertensive disease of pregnancy, delayed onset and protracted labor. Following parturition, cases of retained afterbirth, post parturition hemorrhage and sometimes death occur. An ethno-botanical survey was undertaken in Kathiani and Kyevaluki sub locations of Machakos district to obtain information on the use of medicinal plants during pregnancy, after parturition and their possible effects on uterine muscle. Based on preliminary studies and Traditional Birth Attendants (TBA) questionnaire analysis; two plants *Ricinus communis* and *Euclea divinorum* were identified for further laboratory studies. Aqueous, ethanolic and chloroformic extracts of the root bark of both plants were prepared. The effect of the extracts on isolated uterine strips was investigated both in the presence and absence of oxytocin and prostaglandin F2α. The uterine strips were exposed to a range of serial extract concentrations: (0.5 to 4.0 mg/ml). The data was analyzed using ANOVA, P values $< 0.05$ were considered significant.

A total of 200 TBAs were interviewed and 57 medicinal plants identified and documented. Twenty plant species were used for the management of delayed and protracted labor, 17 for post partum hemorrhage, 9 for stimulation of milk ejection, 50 for the prevention of abortion, 20 for the management of vomiting and 38 for the treatment of pregnancy edema and anemia. All uteri exhibited a strong initial contraction following exposure to the aqueous and ethanol extracts, in a dose dependent manner. Upon recovery the frequency (contractions per second) varied with the plant extract. In the absence of hormones, the frequency of uterine contraction in non pregnant strips ranged between $1.46 \pm 0.05$ to $1.61 \pm 0.02$ for aqueous *Euclea*

*divinorum* root bark extract, 2.1 ± 0.41 to 2.61 ± 0.53 for aqueous *Ricinus communis* extract, 2.36 ± 0.31 to 2.69 ± 0.66 for ethanol *Euclea divinorum* extract and 2.8 ± 0.41 to 2.93 ± 0.08 for ethanol *Ricinus communis* extract. The presence of oxytocin and prostaglandin F2α in non pregnant uteri caused a contraction frequency that ranged between 1.616 ± 0.01 to 1.81 ± 0.02 for aqueous *Euclea divinorum* extract, 5.58 ± 0.14 6.54 ± 0.12 for aqueous *Ricinus communis* extract, 3.23 ± 0.31 to 4.13 ± 0.21 for ethanol *Euclea divinorum* and 3.89 ± 0.25 to 4.57 ± 0.32 for ethanol *Ricinus communis* extracts. In the absence of hormone, the frequency of uterine contraction in pregnant uteri ranged between 1.61 ± 0.34 to 2.22 ± 0.49 for aqueous *Euclea divinorum* extract, 3.9 ± 0.51 to 5.86 ± 0.44 for aqueous *Ricinus communis* extract, 2.64 ± 0.06 to 3.62 ± 0.13 for ethanol *Euclea divinorum* extract and 3.77 ± 0.17 to 4.1 ± 0.31 for ethanol *Ricinus communis* extract. The presence of oxytocin and prostaglandin F2α in pregnant uteri caused a contraction frequency that ranged between 13.68 ± 0.53 to 15.42 ± 0.93 for aqueous *Euclea divinorum* extract, 6.5 ± 0.49 to 8.77 ± 0.47 for aqueous *Ricinus communis* extract, 6.32 ± 0.26 to 8.42 ± 0.23 for ethanol *Euclea divinorum* extract and 4.06 ± 0.38 to 4.46 ± 0.34 for ethanol *Ricinus communis* extract. Both chloroform *Euclea divinorum* and *Ricinus communis* extracts exhibited an initial long relaxation phase followed by sharp contractions of the uteri. The result of this study indicate that the crude and ethanolic extracts of the root bark of both plants contained one or more active principles with agonist activity on the uterine oxytocic and prostaglandin F 2α receptors. The results show that the aqueous *Euclea divinorum* root bark extract was more potent than aqueous *Ricinus communis*, ethanol *Euclea divinorum* and ethanol *Ricinus communis* extracts and provides justification for the ethnic use of both plants as oxytocic agents in the initiation of labour, treatment of prolonged labour, post partum hemorrhage and retained placenta. Further pharmacokinetic studies are

required to determine the active principles, possible mechanisms of action, efficacy and safety margins of the plant extracts.

# CHAPTER ONE

## 1.0 INTRODUCTION

Globally, pregnancy and child birth mean unnecessary suffering, ill health or death for more than 30 million women annually, More than 500,000 women die annually of pregnancy related complications, eighty six percent from sub Saharan Africa (WHO, 2003). 150,000 of the maternal deaths result from bleeding complications (Satoko et al., 2006, De Bernis et al., 2003). Each death is a tragedy and collectively, they leave millions of children motherless (WHO, 2003). Maternal mortality due to pregnancy and child birth related complications remains unacceptably high in Kenya at 590 per every 100,000 live birth (NHSSP 2005-2010). Long distance to health facilities, inadequate numbers of staffs and lack of adequate skills amongst the reproductive health workers are some of the contributing factors towards the slow progress in reducing maternal morbidity and mortality in Kenya (NHSSP 2005-2010). Given this scenario, and considering that there are traditional beliefs that certain kinds of herbal plants are beneficial to pregnant women (Ong, 2005), it is no wonder that herbal medicine practice still has a place in Kenya. In rural parts of Kenya, TBAs continue handling and treating pregnant women using medicinal plants. However the efficacy of most traditional herbs used for reproductive health management is largely unproven and their safety is yet to be established. In literature, few data exists regarding the epidemiology and pattern of usage of these herbs during pregnancy (Ong, 2005). Few studies have been undertaken to document the potential benefits of herbal medicine during and after pregnancy and the possible long term adverse effects to the fetus.

The aim of this study was to find out the scientific basis for the use of *Euclea divinonorum* and *Ricinus communis* as prenatal herbal drugs in Machakos and Kangundo districts of Kenya. The various reproductive health issues including pregnancy and post partum complications managed by TBAs were documented and medicinal plants used in their management identified. The *in vitro* effects of *Euclea divinonorum* and *Ricinus communis* on isolated rabbit uterus was consequently investigated.

Based on preliminary studies and analysis of data from the TBA interviews, two plants (*Euclea divinonorum* and *Ricinus communis)* were identified as two of the commonly used plants for induction of labour, treatment of post partum haemorrhage and retained after birth. The antenatal medicines were prepared as infusions or decoctions in Machakos and Kangundo districts.

## 1.1 *EUCLEA DIVINORUM*

The plant belongs to the family *Ebenaceae*. It is an evergreen shrub that grows to a height between 3-5 metres and forms dense foliage. It is widely distributed throughout Kenya in sub humid and semi arid bush land, woodland and in upland forests. It grows in areas 0-2500 metres above sea level, most commonly found between 1400 and 2200 m. In lowlands it mostly grows near water courses especially on black soil (Plate1). *Euclea divinorum* is traditionally used for firewood and walking stick (Kokwaro, 1993). The bark is added to soup as an appetizer and the branches used as tooth brushes (Kokwaro, 1993). The root, bark and leaves have been used for medicinal purposes (Kokwaro, 1993). It is referred to as mukinyai, mukithi, nginyai (fruit) by the Kamba, mukinyei by the Kikuyu, muswa by Luhya and olkinyei by the Maasai (Kokwaro, 1993).

## 1.2 *RICINUS COMMUNIS*

The plant belongs to the family *Euphorbiaceae*. The tree or shrub is probably indigenous to tropical Africa and grows to a maximum of 5 metres. It belongs to a genus with only one species but many varieties (Plate 2). In Kenya it grows over a wide range of altitudes and habitats preferring humus rich, disturbed soil especially along streams. The root, stem, oil from leaves and seeds are reported to have medicinal properties (Kokwaro, 1993). The Kamba local name for the plant is kyaiki or mwaiki; Giriama: m'bono kikuyu: mwariki, Luhya: libono or mubonebone, Luo: Odagwa or Obala dagwa, Maasai: Oldule or Orpaliki, Swahili: bonoo or mbariki and Digo: Mwono (Kokwaro, 1993).

## 1.3 LITERATURE REVIEW

### 1.3.1 Gestational physiology

Fertilization initiates the hormonal mechanisms that are involved in the maintenance of the pregnancy. It is believed that the trophoblast cells of the chorion start secreting human chorionic gonadotrophin (hCG) on the fifth or sixth day after fertilization. The hCG is thought to play a role in the uterine quiescence during gestation (Doheny et al., 2003) through potent concentration dependent inhibitory effect on the myometrial contraction (Slattery et al, 2001). The myometrial contraction inhibition by hCG could be due to direct reduction of intracellular calcium ions (Eta et al., 1994) and down regulation of myometrial gap junctions. HCG is important in the maintenance of the corpus luteum, which will continuously secrete estradiol and progesterone. The role of progesterone in the maintenance of pregnancy has been recognized for more than one hundred years (Csapo and PintoDantas, 1965). The uterine muscles are relatively inactive throughout the gestation period thus maintaining the developing fetus within a tranquil cavity. For labor to be initiated at term, the progesterone block has to be removed (Pieber et al., 2001) through down regulation of hCG receptor concentration (Zuo et al., 1994). In some mammals (rabbit), the main source of progesterone is the corpus luteum throughout gestation. Shortly before labor, luteolysis of corpus luteum occurs causing a reduction in progesterone levels. In other mammals, the corpus luteum plays a major role in progesterone secretion in the first trimester. This function is then taken up by the placenta (Haluska et al., 1994). At term the mechanisms that are thought to play a role in progesterone reduction levels are; loss of progesterone receptors within the myometrium, changes in receptor isoform expression, binding of free active form of progesterone to high affinity protein and metabolism of progesterone to estrogen (Westphal et al., 1977;

McGarrigle and Lachelin, 1984). The complexity of the gestation period therefore makes it sensitive to physiological changes induced by chemical compounds taken during pregnancy. Maternal and newborn mortality are regarded as sensitive indicators of the entire health system (WHO, 2003) and can be used to monitor general health gains. However, these deaths represent the most serious challenges to achieving two of the Millennium Development Goals (MDGs) particularly in sub-Saharan Africa. Nearly all maternal deaths could be prevented with proper prenatal and postnatal care along with skilled attendance at childbirth (WHO, 2003) and the availability of emergency care for serious complications. In rural parts of sub-Saharan Africa access to well equipped health facilities is a major challenge to pregnant women (WHO, 2003). The five major maternal conditions that account for an estimated 75 percent of maternal deaths in Africa are hemorrhage (25%), sepsis (15%), hypertensive disorders of pregnancy (12%), obstructed labor (8%), unsafe abortions (7%) and 20% due to other indirect causes (African Region Health Report 2006).

### 1.3.2 Gestation and post partum complications

Pregnancy induced hypertension is the occurrence of a blood pressure of 140/90 mm Hg or more on at least two occasions four hours apart after the 20th week of pregnancy in a woman known to be normotensive. Usually this kind of pregnancy induced high blood pressure returns to normal by the sixth week postpartum. When proteinuria of 500 mg/l or more is present along with hypertension, the condition is referred to as pre-eclampsia (Davey, 1986). In sub-Saharan Africa, pre-eclampsia occurs in 10% to 20% of pregnant women and the symptoms include headache, vertigo, visual disturbances, vomiting and protenuria. It occurs unexpectedly in about 1 in 2000 maternities in the United Kingdom (Douglas, 1994) and is

therefore difficult to study systematically. More than one third of cases occur before the classic warning signs of both proteinuria and hypertension have been documented, and 44% occur post partum. Thus, the relation between eclampsia and pregnancy induced hypertension and pre-eclampsia is still controversial. Past research shows that if the hypertensive disorder is left untreated it becomes severe and the patient may die within two days post partum (Douglas, 1994). Clinical experience suggests that many women who develop pregnancy induced hypertension in the second trimester will show steadily worsening hypertension, accompanied by the development of proteinuria, thrombocytopenia, failing renal and hepatic function that defines pre-eclampsia. If the disease starts later, pre-eclampsia may never supervene. The fact that late onset pregnancy induced hypertension is not associated with a worse outcome for the fetus than normotension (Paige et al, 1976) taken together with the high incidence of the condition, suggests that it begins as a physiological response to an underlying problem, presumably of fetoplacental perfusion. Angiotensin II stimulates the synthesis of vasodilators such as nitric oxide (Toda et al., 1984) and prostacyclin in the uterus (Broughton, 1988). The pregnant uterus contains an autonomous renin-angiotensin system, and in pregnancy induced hypertension angiotensin II is released into the venous circulation and is present in higher concentrations in the peripheral circulation (Broughton, 1988). One hypothesis is therefore that impaired uteroplacental blood flow in pregnancy induced hypertension stimulates the uteroplacental renin angiotensin system, which both increases peripheral vascular resistance and perfusion pressure directly and also stimulates vasodilator synthesis within the pregnant uterus, allowing increased perfusion. The fact that the administration of angiotensin converting enzyme inhibitors to pregnant women lowers maternal blood pressure (Broughton, 1988) supports this hypothesis.

1.3.2.1 Obstructed labor

Any pregnant woman who is unable to deliver naturally after a full term pregnancy is said to have obstructed labor (Shahida et al, 2003). Such patients usually present at health centres unbooked, brought late when most likely membranes have already ruptured and are exhausted. The majority of women with obstructed labor have a history of not attending antenatal clinic, are of low socio economic status (Rastogi and Trevidi., 1989) and reside in rural areas. The most likely causes of the obstructed labor are cephalo-pelvic disproportion and malpresentation of the fetus (Shahida et al, 2003).

1.3.2.2 Protracted labor

Labor is said to be protracted when the cervix dilation and fetal descent are slow ( less than 1cm / hour). Slow labor might be caused by maternal pelvis being too small, fetus being too large (greater than 5000g) or fetal malpresentation. It might also be due to hypo or hypertonic uterine contractions.

1.3.2.3 Prolonged labor

Prolonged labor occurs when duration of both first and second stage labor exceeds eighteen hours. It is mostly seen in first pregnancies and in women who are over 35 years. Women with prolonged labor usually have fetal malpresentation, cephalo pelvic disproportion, dsyfunctional uterine contractions caused by twins, hydraamnios and / or presence of fibroids. Prolonged labor could also occur due to cervical dystocia or stenosis as a result of previous injury or surgical procedure. Prolonged labor could cause serious morbidity in the woman such as rupture of uterus, rupture of fetal membranes, distressed fetus, exhaustion, increased

pulse rate, dehydration and uterine atony leading to post-partum hemorrhage and or post - partum infection. Proper handling and management of prolonged labor minimizes future reproductive morbidity due to infections.

1.3.2.4 Post-partum hemorrhage

Post partum hemorrhage is the single leading cause of maternal mortality and morbidity in developing countries and a concern in developed countries (WHO, 2003). More than half of all maternal deaths occur within 24 hours of delivery, mostly from excessive bleeding. Every pregnant woman may face life-threatening blood loss at the time of delivery. Women with anemia are particularly vulnerable since they may not tolerate even moderate amounts of blood loss. Therefore every woman needs to be closely observed and if need be, stabilized during the immediate post partum period. Active management of the third stage of labor has been proven to reduce the incidence of post-partum hemorrhage (PPh). Active management of the third stage of labor consists of interventions designed to facilitate the delivery of the placenta (afterbirth) by increasing uterine contractions and preventing PPh through averting uterine atony. Normally, contraction of the uterine arteries compresses the vessels and reduces flow thereby reducing chances of excessive bleeding. In health centers PPh management is achieved through administration of uterotonic agents, controlled umbilical cord traction and abdominal massage. It is therefore important for national health professionals to advocate for skilled care at birth, educate the public on the need for adequate prevention and treatment of post-partum hemorrhage, incorporate active management of the third stage into the curricula for all skilled birth attendants and collaborate with national pharmaceutical regulatory agencies, policy makers and donors to ensure a consistent supply of uterotonics in hospitals.

1.3.3 Physiology of parturition

Parturition is characterized by a complex interplay of paracrine / autocrine factors and signaling molecules within intrauterine tissues (Keelan et al., 1997). At term there is a sudden disruption of the maternal-fetal exchange. This is accomplished with significant degree of danger to both mother and fetus. The mammalian uterus comprises an outer myometrium and an inner endometrium layer (Veale et al., 2000). Uterine myometrial cells are responsible for contraction of the uterus whereas endometrial cells are secretory and non contractile. Prostaglandins are synthesized in both tissues but mainly in the endometrium from where they diffuse into the myometrium without entering the vascular system (Fuchs, 1987). The myometrium consists of circular and longitudinal muscles which differ in structure, function and contraction patterns. During parturition the myometrium contracts rhythmically and forcefully (Kimura et al, 1999).The highly coordinated pattern of contractions aid in dilating the cervix and expelling the fetus and placenta. The contractions are induced by the secretion of oxytocin from the posterior pituitary gland. Oxytocin has clinically been used to initiate labor (Theobold et al., 1948) as well as manage cases of post parturition hemorrhage. The levels of oxytocin and oxytocin receptors in the myometrium have been found to be higher at term than at other periods (Fuchs et al., 1982). Oxytocin plays a crucial role in the expulsive stage of labor and the involution of the uterus (Mitchell et al., 1998). Within seconds of oxytocin stimulation, there is a markedly increased intracellular production of prostaglandins by the myometrium and endometrium. Prostaglandin then potentiates labor through the contraction of the myometrium. The uterine contraction in turn stimulates increased secretion of oxytocin. It is thought that the concentration of oxytocin receptors within the myometrium increases dramatically during gestation and consequently the sensitivity of the uterus to

oxytocin increases as a result of the increased receptors whose synthesis is stimulated by estrogen. In some mammals, the concentration of estrogens and progesterone drop prior to parturition and this is thought to contribute to the removal of the progesterone block to myometrial quiescence.

## 1.4 HERBAL REMEDIES IN REPRODUCTIVE HEALTH

Traditional medicine is used globally and is almost the exclusive source of primary health care for 65% of the world population (Farnsworth, 1994). In developing countries herbal remedies are widely administered to women by TBAs during and after pregnancy (Kokwaro and John., 1998). From an evolutionary perspective use of herbal medicine is an adaptive human behavior (John., 1999). A series of surveys conducted in Finland suggested that, between 1985 and 1988, the use of herbal medicine products during pregnancy rose from 4% to 15% (Hemminki et al., 1991). An Australian survey of three hundred women attending antenatal clinic suggested that 12% had taken herbal medicine during their pregnancy ( Pastore, 2000) while a survey conducted in Nigeria on 1200 pregnant women demonstrated that 12% used native herbs (Gharoro and Igbafe, 2000). A study conducted in South Africa showed that out of 229 pregnant women interviewed 55% had used herbal medicine during pregnancy (Mabina et al, 1997). In the USA, a survey of 200 pregnant women demonstrated that 15% used home remedies (ginger, chamomile, and cola) in an attempt to relieve morning sickness (Pastore, 2000). Despite widespread usage of herbs by pregnant women worldwide and in rural parts of Africa, minimal research findings are available on bioactive components and safety margins of these products. During the last decade, there has been a dramatic rise in the availability and use of medicinal preparations in both developed and developing countries.

Very many people are seeking out various types of natural remedies on the assumption that "natural means safe". In developed countries most of the herbal remedies are classified as dietary supplements and manufacturers are therefore not required to provide proof of efficacy and safety before selling the herbs (Ernst et al., 2001).

Herbs offer potential physiological and psycho-social benefits (Astin, 1998). Health care providers can neither stop nor ignore the use of herbs during pregnancy. Rather they should become informed about the actual properties of herbs used during pregnancy (Astin, 1998). In this way they will be better prepared to advice on when and which herbs should be truly avoided, and on those that pregnant women can continue to use. In North America, the major tonic taken during pregnancy is red raspberry leaf, which is consumed as tea by thousands of pregnant women each year, no adverse events related to its use have been reported (Timothy and Lindi, 2003). In developing countries a lot of research is being done to establish the pharmacokinetics of medicinal herbs especially in dealing with malaria, tuberculosis, HIV/AIDS, cancer and other ailments. Minimal research is being done on herbal remedies in pregnancy (12$^{th}$ Symposium of The Natural Product Research Network for Eastern and Central Africa held in Uganda, 2007). In reality little is known about herbal remedies employed during pregnancy. Data about the safety and efficacy of medicinal herbs is limited. In some cases, the best data is several years old and sometimes only limited to *in-vitro* or animal studies. Clinically important information is sparse in the literature, for example negative trial results, drug interactions, effects in children and / or pregnant and lactating women is lacking. Information about the effects of long term use is usually based on case reports rather than prospective studies. Patients are often unaware of drug interactions, failing

to recognize that herbs are composed of bioactive compounds, some of which may be toxic; others may interact with prescribed medicine altering their effect. Unlike African countries, burgeoning interest in medicinal herbs has increased scientific scrutiny by developed nations on the therapeutic potential and safety of commonly used medicinal herbs, thereby providing physicians with data to help patients make wise decisions about their use (MaryAnn et al, 1998). Popular use of medicinal herbs makes it necessary for physicians to become aware of their health benefits, risks, and uncertainties so that they can educate their patients about their use. In developing nations pregnant women especially from rural areas attend antenatal clinics and at the same time routinely consult traditional birth attendants. More often than not they are given medicinal herbs to alleviate some of the common pregnancy complications. It is known that Kenyan rural women routinely ingest herbs even when pregnant, however statistics on the prevalence of consumption and pattern of use is lacking. The data that has been reported does not distinguish pregnant women from other users. In developed nations, part of the research carried out on the plants commonly used during pregnancy revealed, negative effects on the fetus (Newall et al., 1996). Plants that should be avoided encompass well known hepatotoxins including those containing pyrrolizidine alkaloids and others such as germander, chaparral, European pennyroyal and American pennyroyal (Newall et al., 1996). Oxytoxic and uterine stimulating herbs that may potentially induce spontaneous abortion include; aloes, blue and black colosh, chamomiles, golden seal, American pennyroyal, parsley, rosemary, rue, tansy, chaste tree and castor. American pennyroyal is a known abortifacient. Agnus castus a plant with estrogen like activities used for gynecological problems particularly in Europe is reported to have caused a derangement of gonadotrophin and ovarian hormone levels in a woman who took it (Newall et al., 1996). The plant is

believed to have led to over stimulation of the ovary and may increase the risk of miscarriage. Hypertensive effects that may add to the complication of pre-eclampsia was reported for a number of herbs that were ingested during pregnancy including capsicum, blue colosh, ginger, ginseng, licorice and vervain (Newall et al., 1996). Use of coumarin- containing plants such as alfalfa, angelica, dong quai, aniseed and german and roman chamomiles is a concern for those women suffering coagulation disorders during pregnancy. Conventional drugs and medicinal herb interactions are another concern (Fugh-Berman, 2000) and the need for awareness of complications of this nature is no less important during pregnancy than in other contexts. Examples of potentially allergic herbs consumed during pregnancy are found in members of the *umbelliferae* family, specifically angelica and aniseed.

### 1.4.1 Herbal remedies during labor and parturition

The effect of herbs on uterine tissue has been studied for several years (Sullivan., 1963; Bafor et al., 2009). A survey of 500 members of the American College of Nurses suggested that more than half of them employed herbal medicine for the purpose of inducing labor (McFarlin et al., 1999). The herbs most frequently named were blue cohosh (64%), black cohosh (45%), red raspberry leaf (64%), castor oil (93%) and evening primrose oil (60%). It is interesting to note however that there is no compelling evidence of efficacy for inducing labor in all these products (Ernst et al., 2001). In South Africa, decoctions of *Agapanthus africanus*, *Clivia miniata* and several other herbal remedies are used as oxytocic agents in traditional herbal medicines in order to induce or augment labour (Veale et al., 1992; Varga and Veale 1997., Veale et al., 2000). The study by Varga and Veale 1997 involved interviews with 45 traditional healers in rural and urban KwaZulu Natal. The interviews revealed that *Agapanthus africanus* was one of five plants used most often to treat prolonged labour. The

same interviews also revealed that *Agapanthus africanus* was frequently used to treat constipation in pregnancy. *Ficus exasperata* has been found to stimulate an increase in uterine contractility *in vitro* (Bafor et al 2009). This is supported by reports that the leaves of the plant are used by traditional healers in some parts of Africa (Burundi and Nigeria) as oxytocic to facilitate labor and as abortifacients (Baerts and Lehmann, 1991). Ijeh and Ukweni, 2007 also reported that the plant is used traditionally in hastening the expulsion of the placenta in cows after calf delivery and by TBAs in hastening child birth. The leaf extracts of *Ficus exasperata* contains tannins, flavanoids, saponins and cardiac glycosides (Bafor et al., 2009). Tannins are common constituents of medicinal plant extracts and have been reported to have pharmacological actions of their own. For example tannins have been reported to affect calcium availability for the contraction of uterine smooth muscles as well as cardiac muscles (Calixto et al., 1986, Polya et al 1995). Flavanoids on the other hand have been reported to inhibit uterine contractions (Revuelta et al., 1997), while cardiac glycosides have been shown to affect the uterus of various animal species.

## 1.5 JUSTIFICATION OF THE STUDY

Maternal mortality in Kenya is still unacceptably high at 590 per every 100,000 live birth, due to pregnancy and child birth related causes. Approximately 47 percent of women are still delivering at home (NHSSP-II, 2005-2010) without the attendance of skilled reproductive health staff. Most of these deliveries are attended to by TBAs who are and ill equipped to handle obstetric emergencies (WHO, 2003). The Ministry of Health approved and adopted the National Reproductive Health Policy in 2007 and is currently striving to improve the efficiency and effectiveness of health service delivery to all mothers. Meanwhile the coverage of health care by trained personnel remains low especially in rural parts of Kenya. In

Machakos district the doctor/ patient ratio is 1: 62,325 indicating a serious shortage of health personnel (MDDP 2003-2008).

The well known oxytocic agents such as oxytocin, Prostaglandin $F_{2\alpha}$ (PGF2α) and Prostaglandin E (PGE) are strictly regulated and only administered by trained medical staff (Veale et al., 1992). The situation in Africa, especially rural areas is different. The majority of natives still patronize traditional healers and a large percentage of pregnant women still use herbal remedies during pregnancy and child birth as shown by previous studies in Nigeria (Bafor et al., 2010) and in South Africa (Veale et al., 1992). There is therefore a great need for more studies that will determine the potential benefits of phytomedicines as used traditionally, identify bioactive compounds in these herbs, establish their possible mechanisms of action, and elucidate their side effects.

## 1.6 OBJECTIVE OF THE STUDY

The broad objective of the study was to document indigenous herbs used by TBAs for the management of pregnancy and post parturient complications and to study the *in vitro* effect of two of the herbs on isolated rabbit uterine muscle.

### 1.6.1 Specific objectives

i) To document the various pregnancy and post parturient complications managed by TBAs in Machakos and Kangundo districts of Eastern province of Kenya.

ii) To document and identify medicinal plants used by TBAs in reproductive health management in Machakos and Kangundo districts.

iii) To determine the *in vitro* effects of aqueous, ethanol and chloroform extracts of the selected plants on isolated rabbit uterus and identify the most potent extract.

## 1.7 HYPOTHESIS

### 1.7.1 Experimental hypothesis

Medicinal plants used by TBAs in the traditional management of pregnancy and post parturition complications exhibit physiological effect on isolated rabbit uterus.

### 1.7.2 Null hypothesis

Medicinal plants used by TBAs in the traditional management of pregnancy and post parturition complications do not exhibit physiological effect on isolated rabbit uterus.

# CHAPTER TWO

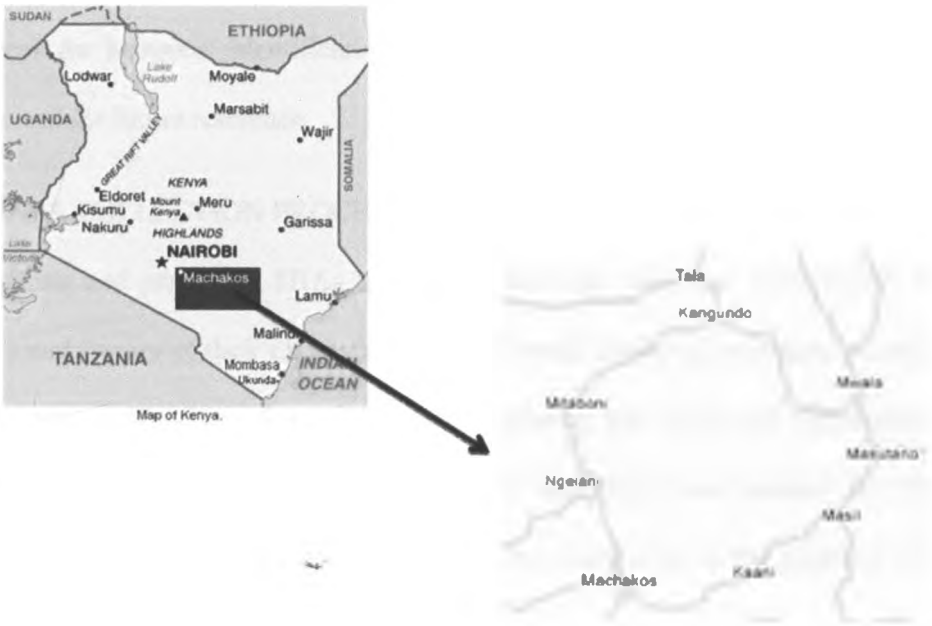
## 2.0 MATERIALS AND METHODS

### 2.1 STUDY AREA

The study was carried out in Machakos and Kangundo districts of the Eastern Province of Kenya as illustrated in figure 1, between July and August 2007. The actual sampling sites were Kyevaluki and Kathiani sub locations which form part of the two hundred and twenty five sub locations of both districts. The districts lie at an altitude between 1000- 1600 meters above sea level and has a total area of 6,281 km² (Machakos District Development Plan 2003-2008). Only 1,574 km² of the total area is under rain fed agriculture. Mean annual rainfall is 1190 mm (500- 1,300 mm) with the high altitude receiving more than lower lying areas. Rainfall is unreliable and varies from year to year. This makes it very difficult for farmers to organize their farming activities (MDDP, 2003). The district has a mean monthly temperature ranging between 12° C in the coldest months to 25° C in the hottest months. According to the Kenya population census report 1999, Machakos district has a total population of 906,644 persons. The numbers are expected to reach 1, 056,535 by the year 2008 (MDDP, 2003). The female population in the reproductive age group (15-49) was 214, 759 in 2002 and is projected to reach 250, 264 by 2008. On the other hand the doctor/ population ratio is 1: 62,325 indicating a serious shortage of health personnel (MDDP, 2003). Despite the district having a hundred and ten health facilities, access to and distribution of these facilities is very poor. This necessitates the rural population to travel long distances (average 5 kilometers) in search of medical services as the health facilities are concentrated in major urban centres. The Machakos district strategic plan (2005-2010) has identified gaps in reproductive health

delivery that need to be addressed. Some of the gaps are lack of adequate skills in reproductive health staff, unsafe motherhood and inadequate access to affordable quality service. The unavailability of public transport at night limits the reproductive service options for most women in labor to the TBAs. Machakos district was chosen on the basis of the high numbers of practicing TBAs and a significant proportion of women still delivering their babies at home. The study area was also close to Nairobi (approximately 150 kilometers away) where the research institution is located.

FIGURE 1: The map of Kenya illustrating the geographical location of Machakos and Kangundo districts. The map shown by the arrow represents the study area: Kyevaluki and Kathiani sub locations.



Map of Kenya.

## 2.2 DOCUMENTATION AND IDENTIFICATION OF MEDICINAL HERBS.

A descriptive cross sectional study of TBAs was carried out in the study area to establish factors that made women consult TBAs during ante partum, intra partum and post partum periods. The questionnaire was pre-tested in Kitui Central District prior to the study. During the study, the questionnaire was used to generate information regarding indigenous knowledge on the medicinal plants used to manage pregnancy associated complications. The method included visiting TBAs to document pregnancy and post partum complications and medicinal plants used to manage/ treat them. Plant parts, route of administration, dose and duration of medicinal plant intake was also documented. Informal conversations, discussions, semi-structured interviews and field excursions were conducted to collect voucher specimens. The plants were harvested and brought to the University of Nairobi, School of Biological Sciences for botanical identification. Voucher specimens were preserved at the university herbarium for future reference.

## 2.3 DATA COLLECTION PROCEDURE

All willing and practicing TBAs residing in the study area were interviewed. Two hundred TBA s and twenty of their clients who had delivered a baby at least three months prior to the administration of the questionnaire were interviewed. The TBAs and client questionnaire are presented as appendices 1 and 2. Face to face interviews were carried out with individual TBA while TBAs focused group discussions were carried out in the presence of their clients. Questionnaires were scrutinized daily and a summary made. The questionnaire provided demographic data on education levels, cultural practices and poverty levels. Dependent

variables were women who had delivered their babies at home whereas the independent variable was cultural practices, poverty and education levels.

2.3.1. Sampling method

Purposive sampling method was used in the two sub locations. All TBAs who met the inclusion criteria (appendix 3) were included in the study.

2.3.2 Choice of sub location

Kyevaluki and Kathiani sub locations were chosen randomly from two hundred and twenty five sub locations of Machakos and Kangundo districts.

2.3.3. Sample size determination

Fisher et al (1998) formula was used to determine sample size. $n = \frac{Z^2 pq}{d^2}$ Whereby n = the desired sample size. Z = the standard normal deviate at the required confidence level p = the proportion in the target population estimate to have characteristics being measured q = 1-p

d = the level of statistical significance set.

2.4 CHOICE OF MEDICINAL PLANTS

From the questionnaire analysis and TBAs focused group discussions, *Ricinus communis* and *Euclea divinorum* were the most commonly used plants by TBAs in the management of delayed labor onset, protracted labor, retained afterbirth and post parturition hemorrhage. The roots of these plants were harvested for further *in vitro* study.

## 2.5 PREPARATION OF PLANT SAMPLES FOR EXTRACTION

Roots of *Euclea divinorum* and *Ricinus communis* were harvested from the study area and brought to the University of Nairobi, Department of Veterinary Anatomy and Physiology. The root bark was removed while the roots were still fresh and cut into small pieces using a knife. The plant pieces were kept under shade and dried at room temperature for a duration of two weeks. The dried root bark was placed in a Cunningham grinder that had both low and high speed. The sample was ground in a fuse chamber using two levels of low speed and one level of high speed each lasting 15 seconds. This was repeated until all the dry sample was turned into powder (Gakuya 2001). The powder obtained was packed in 200 gram portions and placed in clean airtight polythene paper (Gakuya, 2001). To minimize degradation and loss of moisture, the powder was stored in a cool dark area until used.

Plate 1: *Euclea divinorum* plant.

Plate 2: *Ricinus communis* Plant.

## 2.6 DRUGS, CHEMICALS AND EQUIPMENT

Oxytocin (Batch 08D255) and prostaglandin F $2_{\alpha}$ (Batch 663334) hormones were purchased from Agrar and Interchemie laboratories, Holland respectively. Absolute ethanol and chloroform were purchased from British Drug House Company, England. Stilboestral cypionate (batch no. 180903) was bought from Kyron Laboratories Limited in South Africa. Dimethy sulphoxide (DMSO) was bought from Arkema Inc, USA. Glucose (811214) was bought from Pekings Chemicals, China. Sodium chloride (G211907), Potassium chloride (G004206), calcium chloride (G041606), sucrose (G262207), sodium dihydrogen phosphate (G 205901) and calcium hydrogen carbonate (G140706) were bought from Lobachemie laboratory in Holland. A kymograph stimulator and organ bath (plate 4) were purchased from Palmer Bioscience laboratories in USA. The kymograph paper batch number 811-11288-0

was bought from Scientific and Research Instruments limited laboratory, USA. Magnetic stirrer hot plates (HP77STR) were purchased from Wenesco, Inc (Chicago Illinois).

## 2.7 EXTRACTION PROCEDURE

### 2.7.1. Aqueous extraction

Based on preliminary tests 200 grams of *Euclea divinorum* root bark powder was weighed and put in a volumetric flask to which two liters of distilled water was added. The mixture was stirred at room temperature using a magnetic stirrer hot plate until most of the powder had dissolved. This was followed by boiling for ten minutes at 100 ° C (based on preliminary tests). The mixture was left to cool, then filtered using Whitman filter paper and centrifuged at 3000 rpm for ten minutes. The supernatant was subsequently filtered using sintered glass which was able to trap proteins 0.0005 microns in size. The filtrate was subsequently freeze dried for 48 hours. The freeze dried powder was weighed and percentage dry yield was recorded. To prevent moisture uptake the resultant powder was stored in labeled test tubes within a desiccator. The procedure was repeated for *Ricinus communis* root bark powder.

### 2.7.2. Ethanol extraction

200 grams of *Euclea divinorum* root bark powder was similarly weighed and extracted. The extraction was undertaken using a soxhlet apparatus shown in plate 3. The powder was packed in a cellulose 'thimble' which was highly permeable to liquids, (Sahin and Arsla, 2008). The thimble was placed in a central compartment with a siphoning device and a side-arm. The apparatus was fitted into the neck of a flask containing 1500 milliliters of absolute ethanol heated within a water bath. A water condenser was attached to the top of the soxhlet

apparatus. Once the ethanol had boiled, vapor from the solvent reached the soxhlet apparatus through the side tube. The condenser ensured that all solvent vapor cooled, then dripped back into the cellulose chamber dissolving the root bark powder. The solvent / extract mixture filtered through the thimble and back into the flask bearing the ethanol solvent. Exhaustive extraction was carried out by allowing refluxing for 12 hours until a point where no more brown coloration was imparted to the solvent. This point was used as an indication of complete extraction. The continuous extraction method dissolved most of the ethanol soluble active components of the plant. Subsequently the ethanol extract was dried down using a rotary vacuum evaporator in order to remove most of the solvent. The extract was left to further dry at room temperature for 2-3 days in order to ensure complete removal of all the solvent. The dry yield was weighed and stored in labeled test tubes within a desiccator. The procedure was repeated for extraction of *Ricinus communis* root bark powder.

### 2.7.3. Chloroform extraction

Chloroform extraction of *Euclea divinorum* root bark powder was conducted in the same manner as the ethanol extraction except the solvent used was 1500 ml absolute chloroform. The dry yield was weighed and stored in labeled test tubes within a desiccator. The procedure was repeated for R*icinus communis* root bark powder.

## 2.8 ANIMAL WELFARE

Experimental animals were mature, female Swiss white rabbits weighing 1.5- 2.0 Kg. The animals were bought from a licensed breeder (International Livestock Research Institute, Nairobi). The rabbits were transported to the Veterinary Anatomy and Physiology department

animal house and caged separately. Beddings consisted of untreated wood shavings which were changed every other day. The animals were fed on rabbit pellets from Unga feeds Ltd and supplemented with vegetables (kales, carrots and cabbage). Water was provided *ad-libitum*. The animal house was maintained on a 12/ 12 hour light / dark cycle and room temperature maintained at 22 ° C. The animals were handled humanely in accordance with the Institution's Animals Welfare and Ethics Committee guidelines. All the rabbits were allowed to acclimatize for two weeks. The experiment was carried out in the third week of gestation in all pregnant rabbits.

## 2.9 EXPERIMENTAL DESIGN AND TEST SOLUTIONS

A completely randomized design was adopted in the study. Each animal was randomly assigned to an experiment. Similarly, the treatment was assigned randomly to experimental groups. A total of sixty Swiss white rabbits were used in the study. Out of these thirty were picked randomly and mated to yield pregnant uterine tissue. In order to increase the sensitivity of the uterus, all rabbits received 0.1 mg/kg intra peritoneal stilboestral® injection 24-48 hours (Thomas et al, 1995) before the onset of the experiments. Each experiment had a positive control in which the tissue was exposed to Oxytocin and prostaglandin F2α only and a negative control in which de jalon solution alone was used. After the 48 hours, the oestrogenized rabbits were killed by cervical dislocation. The uterine horns were carefully dissected into a dish of de jalon solution (0.5 grams glucose, 9.0 grams sodium chloride, 0.42 grams Potassium chloride, 0.24 grams calcium chloride, 4.5 grams sucrose, 0.142 grams sodium dihydrogen phosphate and 2.1 grams calcium hydrogen carbonate reconstituted in a litre of distilled water). After trimming off the extraneous tissues, the uterine tissue was cut

into strips measuring 30 mm long. Each strip therefore was composed of whole uterine tissue (myometrium and endometrium). The viability of the uterine tissue was maintained by constant immersion in 40 ml de jalon solution which was maintained at 33-35 ° C and constantly gassed with a mixture of 95% oxygen and 5% carbon dioxide. One uterine strip at a time was mounted. The strip was mounted vertically within the organ bath as shown in plate 4, with one end fixed while the other was attached to a force transducer as described by Yoshinobu, (2001). Each uterine strip was allowed to stabilize for twenty to thirty minutes after which relaxation and contractions of the uterine strip were recorded on a kymograph paper at a constant 'kymograph' speed of 20 mm per second for at least five minutes negative control).

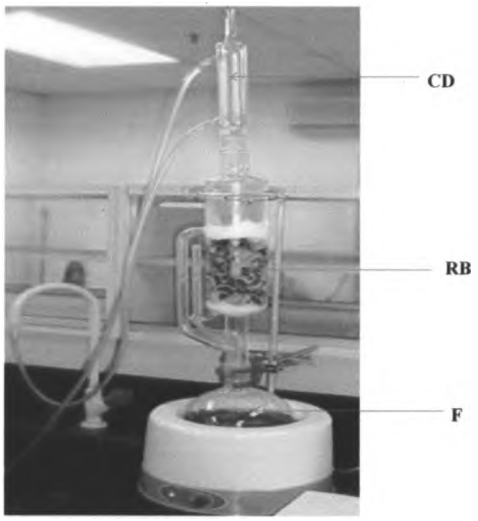



**Plate 3**: The soxhlet apparatus.

KEY: CD- condenser RB-Root bark powder of the plant. F- Flask containing absolute ethanol or chloroform.

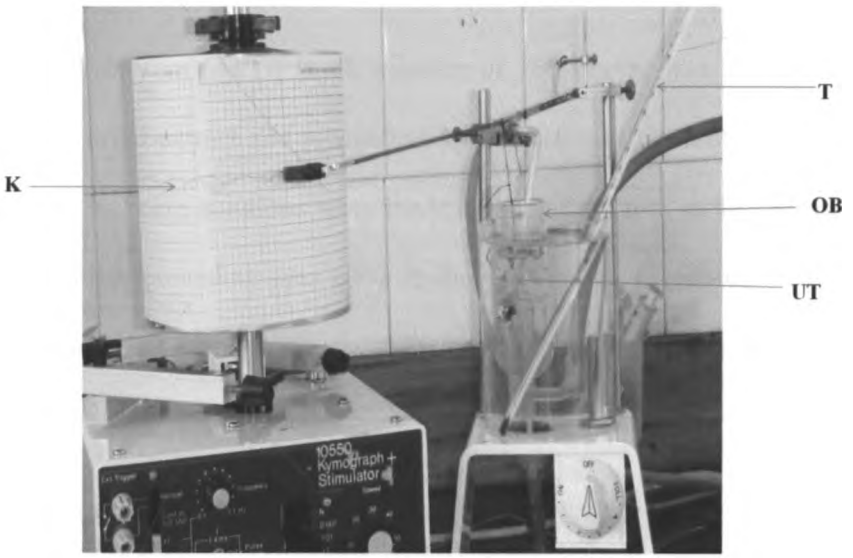



**Plate 4:** Kymograph+ stimulator and organ bath set up.

KEY: K- kymograph paper. OB- organ bath chamber UT- uterine strip suspended vertically in the organ bath. T- thermometer:

2.9.1 Aqueous and ethanol extract stock solutions

Aqueous *Euclea divinorum* (AED) stock solution of 160 mg/ml was prepared by weighing 1600 mg of freeze dried extract and reconstituting with 10 milliliters of distilled water. From the stock solution, working solutions were made by serial dilution at 80, 40 and 20 mg / ml dose levels. A similar procedure was used in the preparation of ethanol E*uclea divinorum* (EED) stock solution as well as aqueous *Ricinus communis* (ARC) and ethanol *Ricinus communis* (ERC).

2.9.2. Chloroform extract stock solution

A similar procedure was used in the preparation of both chloroform *Euclea divinorum* (CED) and *Ricinus communis* (CRC) working solutions except distilled water was replaced by DMSO. From the stock solution serial dilutions were carried out to make 80, 40 and 20 mg/ml dose levels.

2.10 THE EFFECT OF OXT AND PGF2α ON PREGNANT AND NON PREGNANT UTERINE STRIPS (POSITIVE CONTROL).

Non pregnant and pregnant uterine strips were separately mounted and allowed to stabilize for thirty minutes. After the uterine strip had stabilized negative control recordings were taken for 5 minutes. Thereafter the uterine strip was exposed to 1ml OXT in the presence of 0.5ml PGF2α. The effect of OXT with PGF2α was recorded for five minutes in triplicates and this acted as positive controls.

## 2.11 THE EFFECT OF AQUEOUS AND ETHANOL *EUCLEA DIVINORUM* (AED and EED) EXTRACTS ON PREGNANT AND NON PREGNANT UTERINE STRIPS.

The effect of test solutions on the frequency of uterine contraction as well as contraction strength was analyzed. The frequency was taken as the number of contractions recorded over a 5 minute period. The strength of contraction as given by the amplitude was obtained by measuring the difference in contraction amplitude between the negative control section and the 'extract induced' uterine contractions. Each measurement was done in triplicate.

### 2.11.1 Effect of AED extract on non pregnant uterine strips

4.0, 2.0, 1.0, and 0.5 mg/ml extract organ bath concentrations were obtained by adding 1ml of stock solution (160, 80, 40, 20 mg/ml) to 40 ml de jalon solution in the organ bath. A fresh uterine strip was used each time. After the uterine strip had stabilized (twenty to thirty minutes) negative control recordings were taken for 5 minutes. Thereafter the uterine strip was exposed to 0.5 mg/ml AED extract. An incubation time of five minutes was maintained throughout the experiment. Once the isometric contractions were recorded for five minutes, the strip was washed three times with fresh de-jalon solution. The uterine strip was allowed to recover for twenty minutes after which it was exposed to 1.0 mg/ml extract concentration and isometric contractions recorded for five minutes. The process was repeated until the uterine strip had been exposed to all the organ bath concentration range; (0.5, 1.0, 2.0 and 4 mg/ml). A fresh uterine strip was then mounted in the organ bath. The strip was left to stabilize for twenty minutes during which negative control recordings were taken. Immediately after 1 ml of OXT, 0.5 ml PGF 2α as well as 1 ml of 20 mg/ml stock AED extract was simultaneously added to the organ bath solution. The uterine response was recorded for five minutes as

above. Immediately after, the strip was washed three times with fresh de jalon solution and allowed to recover for 20 minutes. While OXT and PGF2α content in the organ bath remained unaltered, the uterine strip was similarly exposed to gradually increasing organ bath concentrations of AED (1.0, 2.0 and 4.0 mg / ml) as before and the responses recorded. In all cases both frequency and strength (amplitude) of contractions were determined as outlined in 2.11.1 above. Each measurement was repeated in triplicate.

2.11.2. Effect of AED extract on pregnant uterine strips

The procedure in 2.11.1 was repeated using 'pregnant uterine strips'.

2.11.3 Effect of EED extract on non pregnant and pregnant uterine strips

The same procedure in 2.11.1 was again repeated using ethanol *Euclea divinorum* extract on non pregnant and pregnant uterine strips.

2.11.4 Effect of chloroform *Euclea divinorum* (CED) extract on pregnant and non pregnant uterine strips

Fresh non pregnant uterine strips were exposed to 0.5 mg/ml of chloroform *Euclea divinorum* extract in absence of oxytocin and prostaglandin F2α. The isometric contractions were recorded for five minutes. The uterine strips were washed with fresh de jalon solution and left to recover for thirty minutes. The strips were then gradually exposed to increasing concentrations of the extract (1.0, 2.0 and 4.0) as outlined in section 2.11.1. This was repeated in the presence of oxytocin and prostaglandin F2α. The same procedure was carried out, with pregnant uterine strips in the presence and absence of OXT and PGF2α.

## 2.12 THE EFFECT OF AQUEOUS AND ETHANOL *RICINUS COMMUNIS* (ARC and ERC) EXTRACTS ON PREGNANT AND NON PREGNANT UTERINE STRIPS

### 2.12.1 Effect of ARC extract on non pregnant uterine strips

4.0, 2.0, 1.0, and 0.5 mg/ml extract organ bath concentrations were obtained by adding 1ml of stock solution (160, 80, 40, 20 mg/ml) to 40 ml de jalon solution in the organ bath. A fresh uterine strip was used each time. Once the uterine strip had stabilized for (twenty to thirty minutes) as before, negative control recordings were taken for 5 minutes. Thereafter 0.5 mg/ml ARC extract was infused into the organ bath solution and isometric contractions recorded for five minutes. At the end of the five minutes, the uterine strip was washed three times with fresh de-jalon solution and again allowed to recover for twenty minutes, after which it was exposed to 1.0 mg/ml extract concentration. Its isometric contractions were then recorded for five minutes. The process was repeated until the uterine strip had been exposed to all the organ bath concentration range; (0.5, 1.0, 2.0 and 4 mg/ml). A fresh uterine strip was then mounted in the organ bath. The strip was left to stabilize for twenty minutes during which negative control recordings were taken. Immediately after 1 ml of OXT, 0.5 ml PGF 2α as well as 1 ml of 20 mg/ml stock ARC extract was simultaneously added to the organ bath solution. The uterine response was recorded for five minutes after which the strip was again washed three times with fresh de jalon solution and allowed to recover for 20 minutes. While OXT and PGF2α content in the organ bath remained unaltered, the uterine strip was similarly exposed to gradually increasing organ bath concentrations of ARC (1.0, 2.0 and 4.0 mg / ml) as before and the responses recorded. Both the frequency and strength (amplitude) of uterine contraction were determined as outlined before in section 2.11. Each measurement was done in triplicate.

2.12.2. Effect of ARC extract on pregnant uterine strips

The procedure in 2.12.1 was repeated using 'pregnant uterine strips'.

2.12.3 Effect of ERC extract on non pregnant and pregnant uterine strips

The same procedure in 2.12.1 was again repeated using ethanol *Ricimus communis* extract on non pregnant and pregnant uterine strips.

2.12.4 Effect of chloroform *Ricinus communis* (CRC) extract on pregnant and non pregnant uterine strips

Fresh non pregnant uterine strips were exposed to 0.5 mg/ml of chloroform *Ricinus communis* extract in absence of OXT and PGF2α. The isometric contractions were recorded for five minutes. The uterine strips were washed with fresh de jalon solution and left to recover for thirty minutes. The strips were then gradually exposed to increasing concentrations of the extract (1.0, 2.0 and 4.0). The procedure was repeated using non pregnant uterine strips in the presence of OXT and PGF2α as described in section 2.12.1.The procedure was also carried out using pregnant uterine strips in the presence of OXT and PGF2α and repeated in the absence of OXT and PGF2α.

2.13 DATA ANALYSIS AND PRESENTATION

2.13.1 Ethno botanical survey

Demographic data for both the TBAs and their clients is presented in the form of bar graphs. Data on medicinal plants used by TBAs in the management of pregnancy and post-pregnancy complications is presented in the form of tables and bar graphs. Questionnaire data was coded using Ms Excel software.

2.13.2 *In vitro* studies

All values were expressed as mean ± standard error of mean (S.E.M). The data was analyzed using One-Way ANOVA and two sided Dunnett post hoc test using SPSS version 11.5.

P-values < 0.05 were considered significant. * denotes P < 0.05, ** denotes P< 0.01 and *** denotes P< 0.001.

# CHAPTER THREE

## 3.0 RESULTS

### 3.1 ETHNOBOTANICAL SURVEY

#### 3.1.1 TBAs data

A total of 200 TBAs were interviewed. One hundred and twenty eight (64%) TBAs were married, fifty eight (29%) were single whereas fourteen (7%) were widowed (Figure 2). 84% of the interviewed TBAs were females. Seventy four (37%) were in the age group 40-50 years, sixty (30%) were in the age group 51-60 years, forty four (22%) were in the age group 61-70 years whereas twenty two (11%) were above 70 years (Figure 3). One hundred and thirty eight (69%) had 4-6 children, fifty four (27%) had 1-3 children and 4% had 7-9 children (Figure 4). One hundred (50%) had never attended school, eighty (40%) had primary level of education whereas twenty (10%) had completed secondary school (Figure 5). Ninety four (47%) had practiced for over five years, fifty (25%) had practiced between one to five years, thirty eight (19%) had practiced for over ten years whereas eighteen (9%) had practiced for less than a year (Figure 6). One hundred and twenty eight (64%) had attended to over 200 patients, forty six (23%) had handled 51- 100 patients and twenty six (13%) had attended to less than fifty patients as shown in Figure 7. One hundred and thirty eight (69%) had acquired the traditional birth attendance skills through family inheritance, thirty six (18%) were trained by practicing TBAs and twenty six (13%) had acquired the knowledge through divine intervention (Figure 8).

3.1.2 Client data

Twenty clients were interviewed. All were females and had delivered at least three months prior to the interview. 60% were married, 25% single and 15% were widowed (Figure 9). 40% were in age group 26-30 years; 25% were 21-25 years old; 20% were between 16-20 years old, 10% were between 31-35 years and 5% were between 36-40 years (Figure 10). 55% had just delivered their first baby whereas 45% had more than one child (Figure 11). 75% of the clients had completed primary level of education, 15% had completed secondary education, 5% had never attended school and 5% had attended college (Figure 12). Figure 13 shows the location where the client delivered their baby. 55% of the clients had delivered at home whereas 45% had delivered in hospital. Among those who had delivered at home, 35% could not afford hospital charges, 35% preferred the readily available TBAs services and 30% had previously been abused by reproductive health workers (RHW) (Figure 14). 35% of the clients consulted the TBAs due to vaginal bleeding, 25% due to delayed labor, 25% due to dizziness and 15% due to lower abdominal pain (Figure 15). All clients took their babies for post natal clinic. 25% took the babies immediately after delivery, 35% two weeks after delivery and 40% one month after delivery (Figure 16). During labor 70% of the clients were helped (physical as well as psycho social support) by the TBAs, 25% were helped by relatives and 5% delivered without any help (Figure 17). 50%, 40% and 10% of the clients had to walk for 2 hours, 1 hour and 30 minutes respectively to get to the nearest health centre (Figure 18). 85% of the clients had access to public transport during daytime only as compared to 15% who had access all the time (Figure 19).

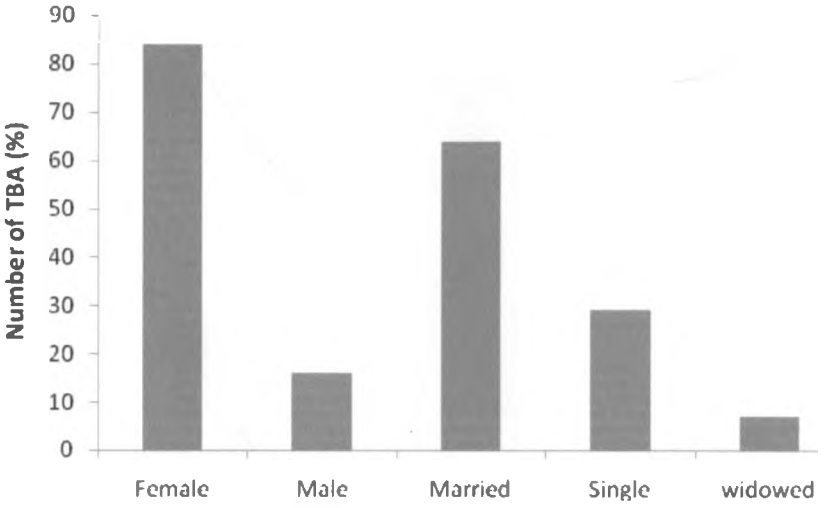



FIGURE 2: Gender distribution and marital status of TBAs.

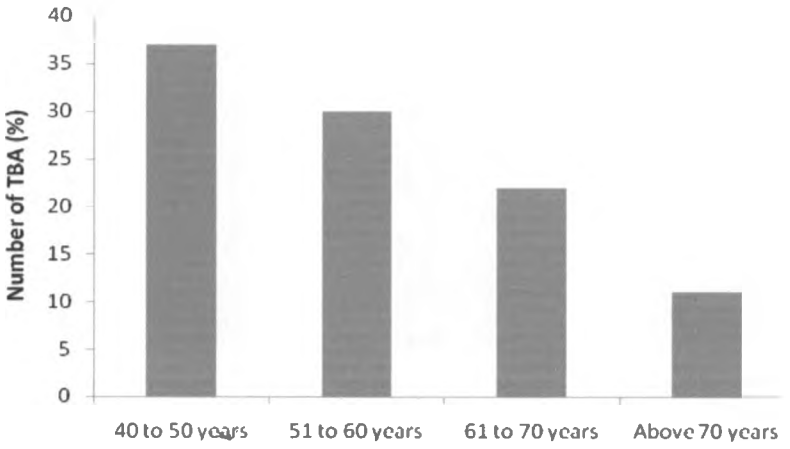



FIGURE 3: Distribution of TBAs per age group.

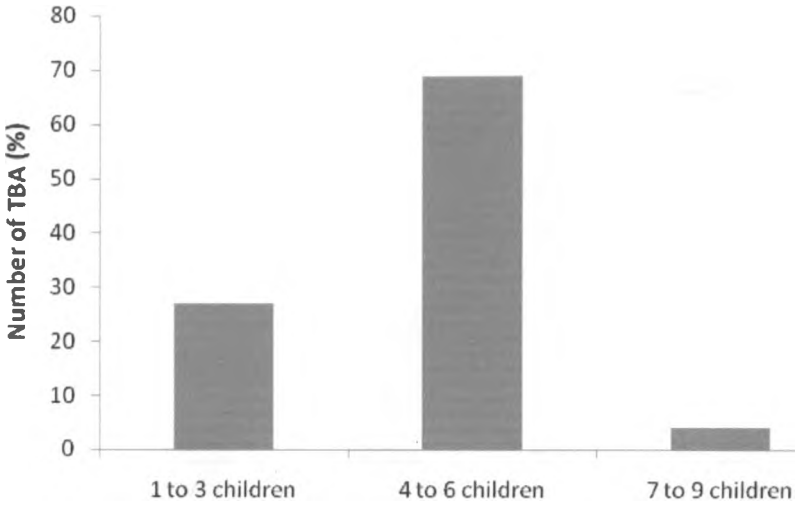



FIGURE 4: TBAs parity levels

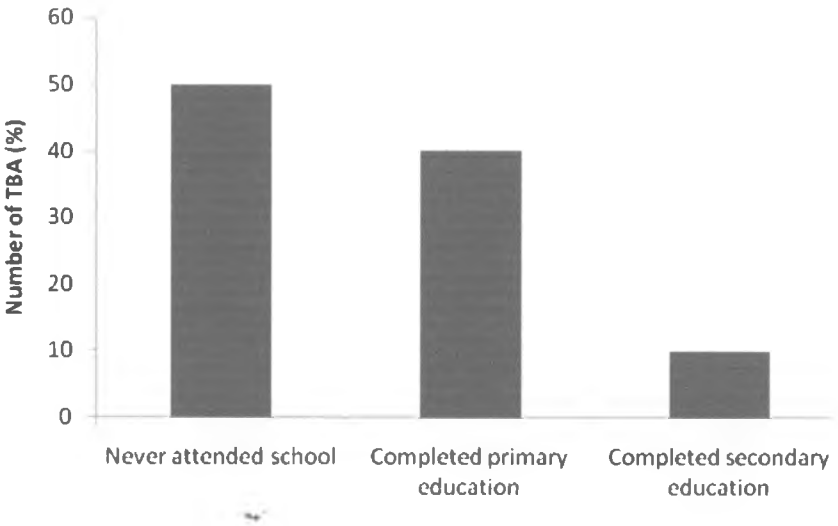



FIGURE 5: Education level disparity among the TBAs.

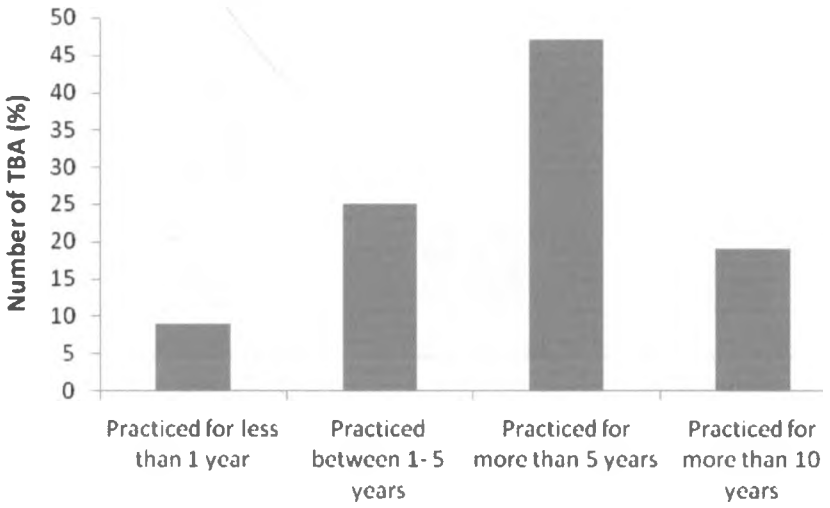



FIGURE 6: TBAs practicing experience in years.

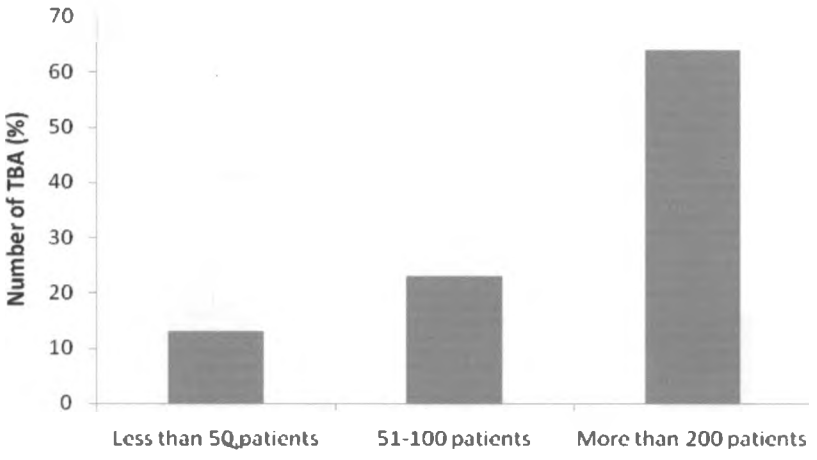



FIGURE 7: Number of pregnant women managed / treated by TBAs.

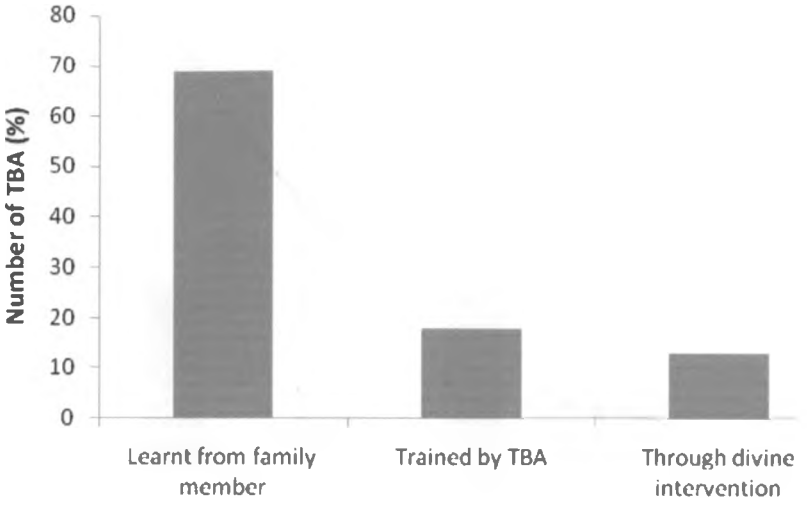



FIGURE 8: Methods used by TBAs to acquire reproductive health skills.

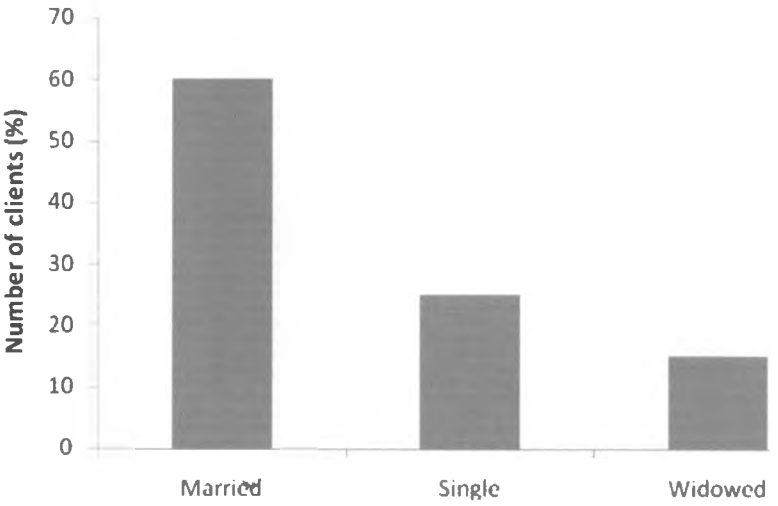



FIGURE 9: 'Client's marital status.

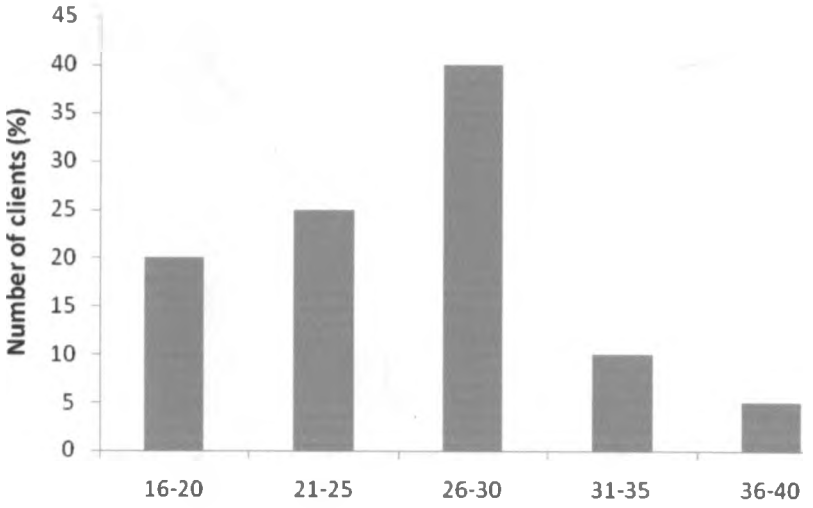



FIGURE 10: 'Client's age groups (years).


FIGURE 11: 'Client's parity levels.

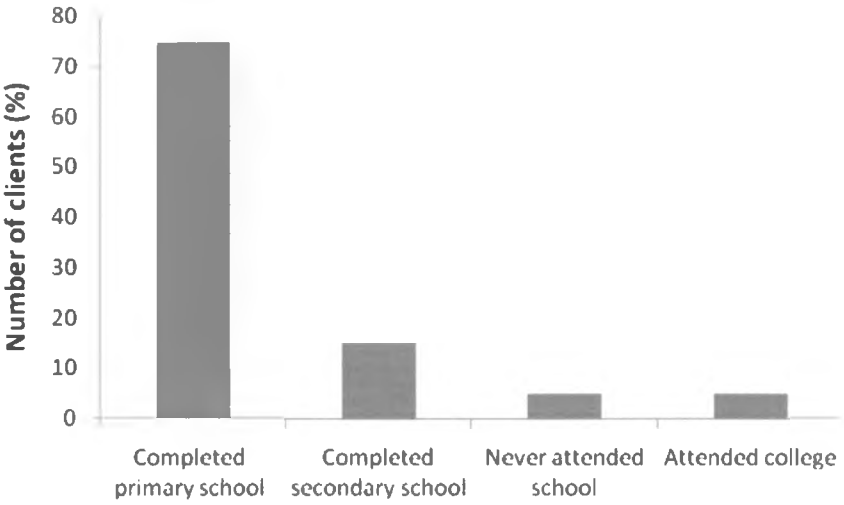



FIGURE 12: 'Client's education levels.

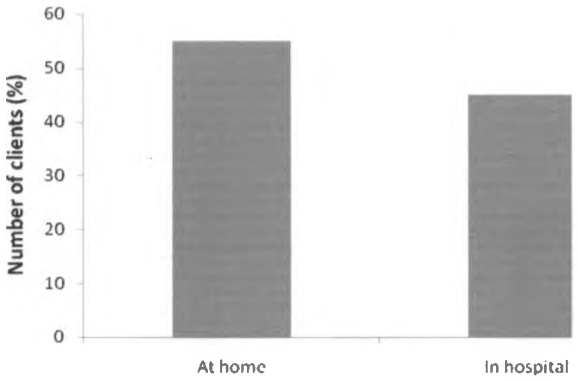



FIGURE 13: 'Client's home verses hospital deliveries.

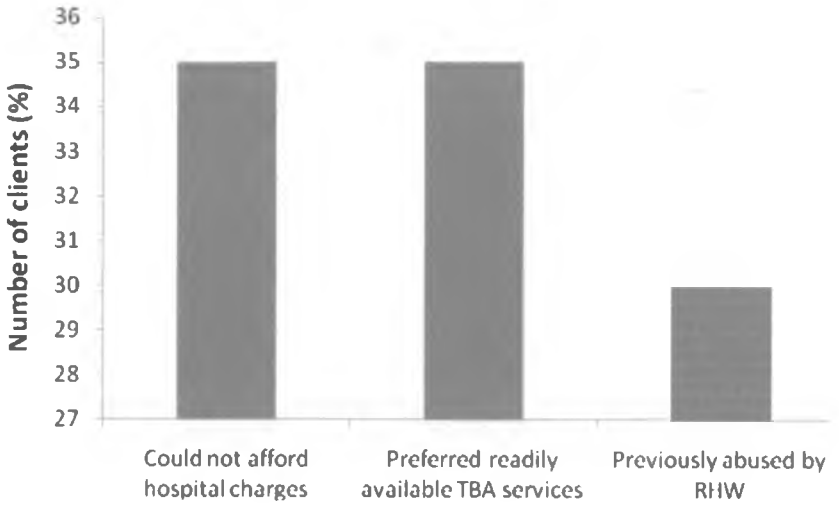



FIGURE 14: 'Client's reasons for the home delivery.

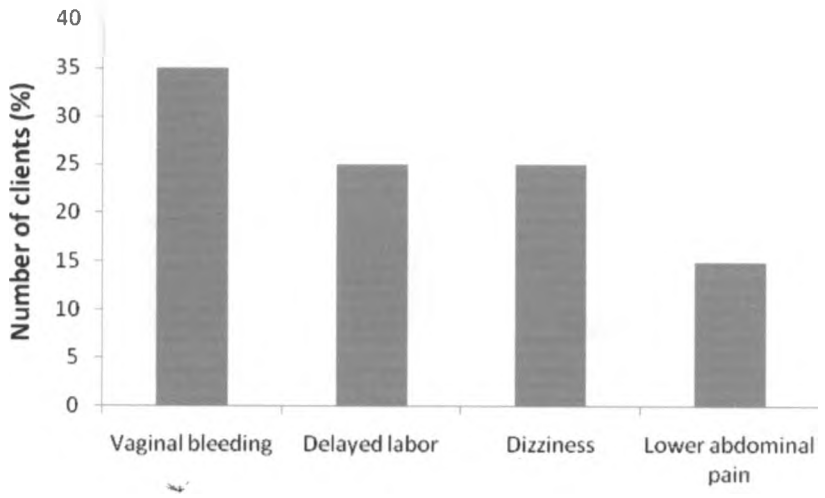



FIGURE 15: Clinical signs during pregnancy that led to TBAs consultation.

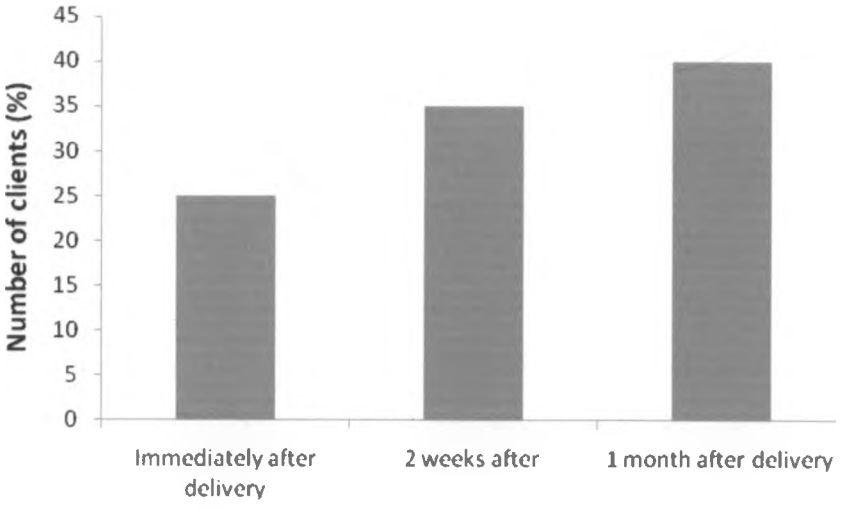



FIGURE 16: 'Client's post natal clinic attendance.

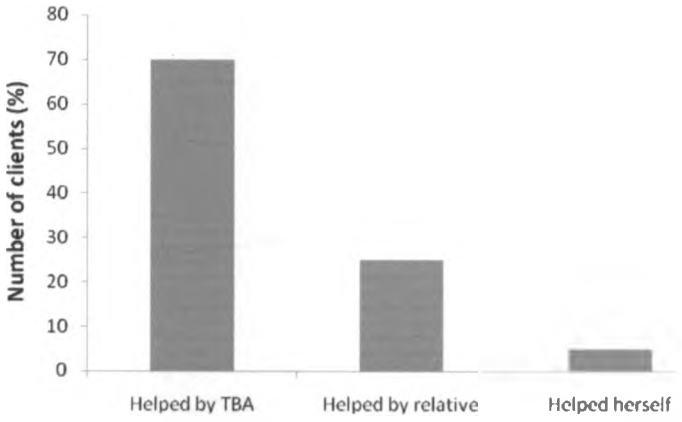



FIGURE 17: Provision of physical and psychosocial support to the client during labor.

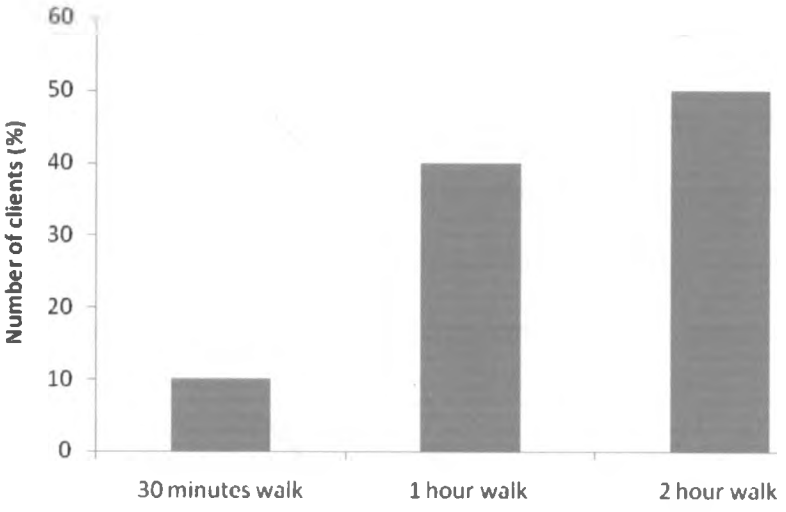



FIGURE 18: The distance to the nearest health centre.

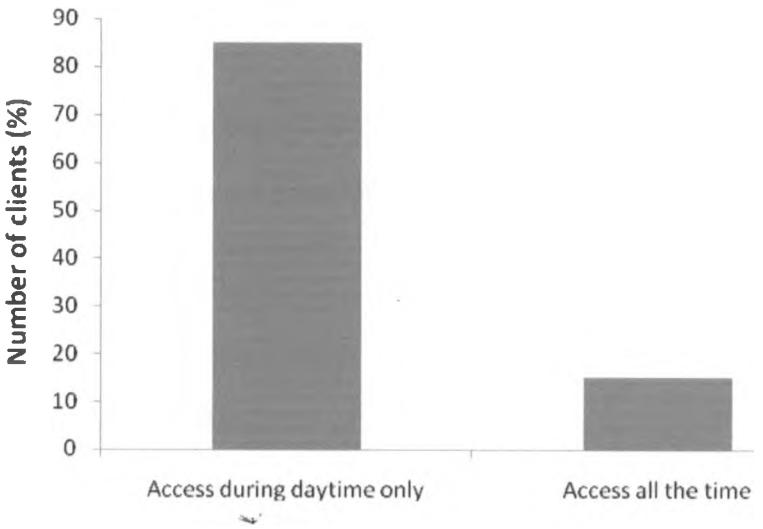



FIGURE 19: Availability of public transport.

3.1.3 Interventions used by TBAs for the management of pre and post partum complications.

In addition to administration of herbal medicine, TBAs used other interventions in the management of pregnancy and post partum complications. Figure 20 to 29 shows the types of interventions used by TBAs for the management of delayed and protracted labor, post-partum hemorrhage, retained after birth, initiation of post partum milk ejection, prevention of first, second and third trimester abortion, vomiting, pregnancy edema and anemia.

3.1.3.1 TBAs management of delayed labor.

55% of the TBAs used herbal remedy in the management of delayed labor, 31% referred patients to hospital whereas 14% used divine intervention (Figure 20).

3.1.3.2 TBAs management of protracted labor

Thirty eight percent administered herbal remedy, 23% referred patients to hospital. 20% combined interventions to manage the condition (administered herbs, massaged the patient's abdomen and prayed). 16% managed protracted labor through prayers (divine intervention) while 3% massaged their patient's abdomen and hoped for a positive outcome (Figure 21).

3.1.3.3 TBAs management of post-partum hemorrhage

62% managed post partum hemorrhage using herbal remedy (Figure 22). 29% referred patients to hospital whereas 9% had never handled such patients.

3.1.3.4 TBAs management of retained after birth

Several interventions were used by TBAs in the management of retained after birth (Figure 23). 56% managed retained afterbirth using herbal remedy, 32% removed the placenta manually. TBAs that administered medicinal plants and removed the placenta manually were

more than those that massaged the lower abdomen (6%), referred patients to hospital (3%) and those that did not handle such patients (3%).

3.1.3.5 Initiation of milk ejection

Interventions used by TBAs for the initiation of milk ejection are shown in Figure 24. 65% administered herbs orally, 32% had never handled such patients and 3% advised their patients on proper nutritional intake.

3.1.3.6 TBAs prevention of first trimester abortion

Interventions used by TBAs for the prevention of first trimester abortion are shown in Figure 25. 63% administered herbs orally, 20% referred their patients to hospital whereas 17% massaged the lower abdomen of their patients.

3.1.3.7 TBAs prevention of second and third trimester abortion

Interventions used by TBAs for the prevention of second and third trimester abortion are shown in Figure 26. 72% administered herbal remedy as compared to 28% who referred the patients to hospitals.

3.1.3.8 TBAs management of vomiting during pregnancy

Interventions used by TBAs for the management of vomiting during pregnancy are illustrated in Figure 27. 55% referred such cases to hospitals, 33% administered herbal remedy whereas 12% had never handled such cases.

3.1.3.9 TBAs management of pregnancy edema

Interventions used by TBAs for the management of edema during pregnancy are shown in Figure 28. 43% administered herbal remedy, 31% did not handle such patients, 15% referred patients to hospitals, 7% massaged affected area and 4% advised their patients on nutritional intake.

3.1.3.10 TBAs management of pregnancy anemia

Interventions used by TBAs for the management of anemia are shown in Figure 29. 64% advised their patients on the importance of balanced diet as compared to 36% who administered herbal remedy.

3.1.4. DOCUMENTATION OF PLANTS

The two medicinal plants chosen for *invitro* studies were (*Euclea divinorum* and *Ricinus communis*). The two were the most commonly mentioned in the questionnaires for the management of delayed labor, protracted labor, post partum hemorrhage and retained after birth. Table 1 to 10 documents the types of medicinal plants used by TBAs for the management of pre and post partum complications. Table 11 and 12 provides examples of medicinal plants administered between one to fourteen days by TBAs for the management of pregnancy complications (edema, vomiting, threatened abortion) and post pregnancy conditions like post partum hemorrhage regardless of the possible adverse effect on the unborn baby and expression of bioactive components through breast milk.

3.1.4.1 Herbs used by TBAs for the management of delayed labor

The herbs were administered to women whose gestation period had exceeded 40 weeks. Ten medicinal plants used by TBAs to induce labor were identified (Table 1). The plants belong to 9 genera and 8 families. All plants were administered orally and the commonest plant part used was the root (40%). Most of the TBAs cleaned the outer surface of root and gave the client to chew. The commonest plants used were *Ricinus communis* and *Euclea divinorum.*

3.1.4.2 Herbs used for the management of protracted labor

Ten medicinal plants traditionally used in the management of protracted labor were identified (Table 2). *Ricinus communis* and *Euclea divinorum* plants were most commonly mentioned by TBAs as being useful in the management of protracted labor.

3.1.4.3 Herbs used for the management of post-partum hemorrhage

Seventeen medicinal plants were identified for the management of post partum hemorrhage (Table 3). The preferred route of administration was oral though a few of the TBAs administered the herbs topically.

3.1.4.4 Herbs used for the management of retained afterbirth

Seven medicinal plants were identified for the management of retained after birth (Table 4). *Ricinus communis* and *Euclea divinorum* plants were most commonly mentioned in the management of retained after birth. The preferred route of administration was oral.

3.1.4.5 Herbs used for the initiation of milk ejection

Nine plants were identified by the TBAs for the initiation of milk ejection (Table 5). All the plants were administered orally. Several plants were used as decoctions for example, *Carisa edulis* and *Fagaropsis hildebrandtii.*

3.1.4.6. Herbs used for the prevention of first trimester abortion

Twenty four medicinal plants were identified for the prevention of first trimester abortion (Table 6). Some of the plants were administered as decoctions. For example *Zanthoxylum, chalybeum, Fagaropsis hildebrandtii* and *Carisa edulis* were ground, mixed and administered orally whereas *Solanum incunum* was applied topically. S*trychnos henningsii, Bosia angustiafolia* and *Hoslundia opposite* plants were mixed then administered orally.

3.1.4.7 Herbs used for the prevention of second and third trimester abortion

Twenty seven medicinal plants were identified for the prevention of second and third trimester abortion (Table 7). The preferred route of administration was oral.

3.1.4.8 Herbs used for the management of vomiting during pregnancy

Twenty medicinal plants were identified as effective in preventing nausea and vomiting as shown in Table 8. The preferred route of administration was oral.

3.1.4.9 Herbs used for the management of pregnancy edema

Twenty eight plants were identified for the management of edema (Table 9). All plants were administered orally regardless of the age of pregnancy. Some of the plants were administered for duration of one to seven days (Table 11).

3.1.5.0 Herbs used for the management of pregnancy anemia

Ten medicinal plants were identified for the management of anemia during pregnancy (Table 10). All the plants were administered orally.

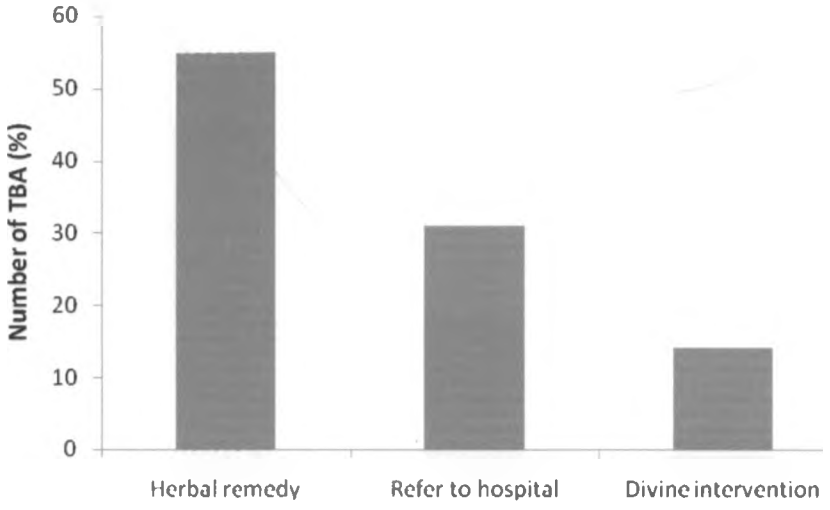



FIGURE 20: Interventions for the management of delayed labor.

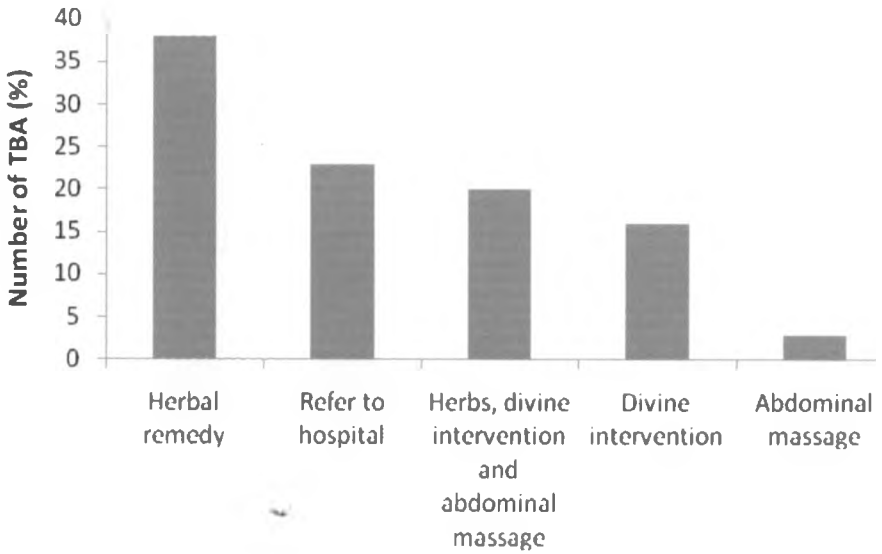



FIGURE 21: Interventions for the management of protracted labor.

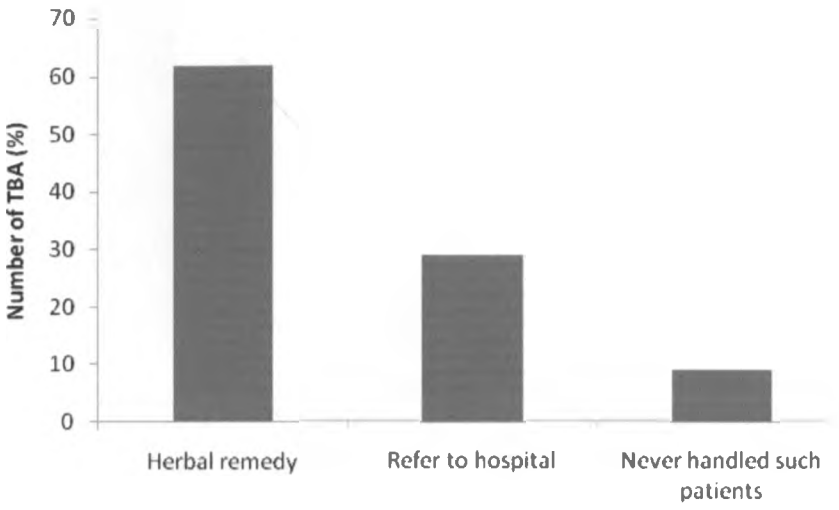



FIGURE 22: Interventions for the management of post partum hemorrhage.

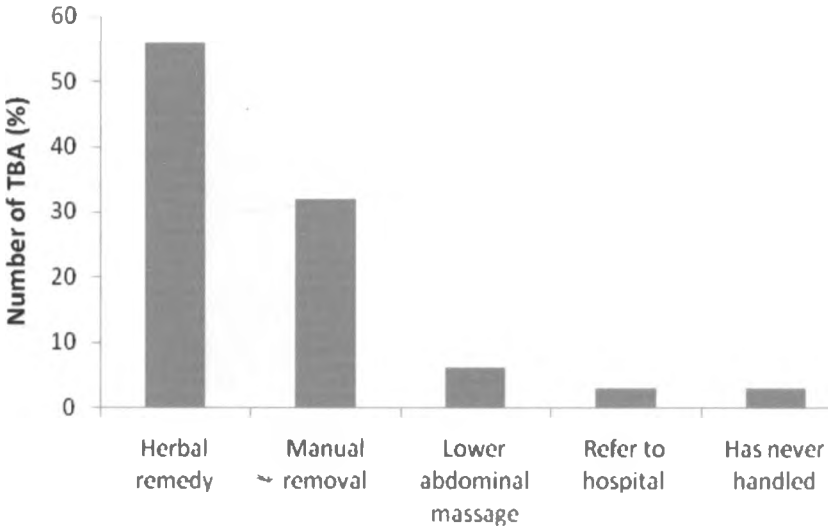



FIGURE 23: Interventions for the management of retained after birth.

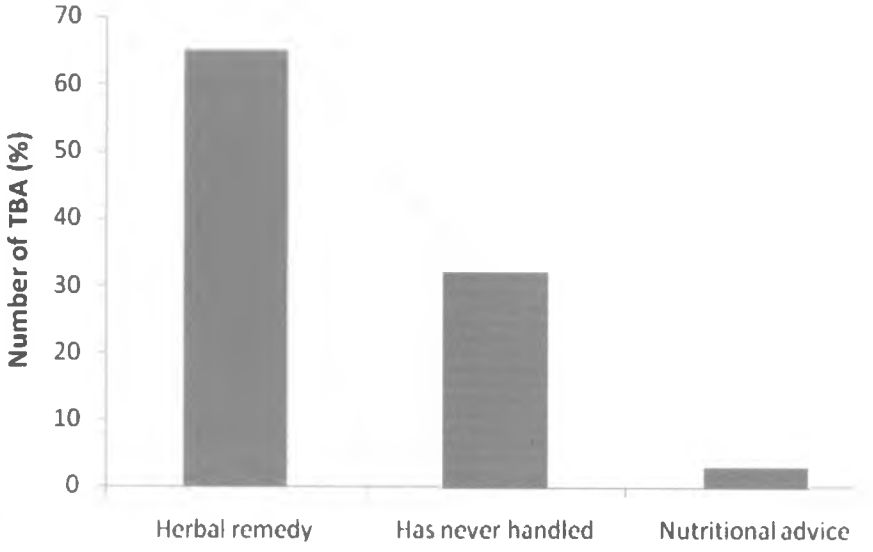



FIGURE 24: Interventions for the initiation of milk ejection.

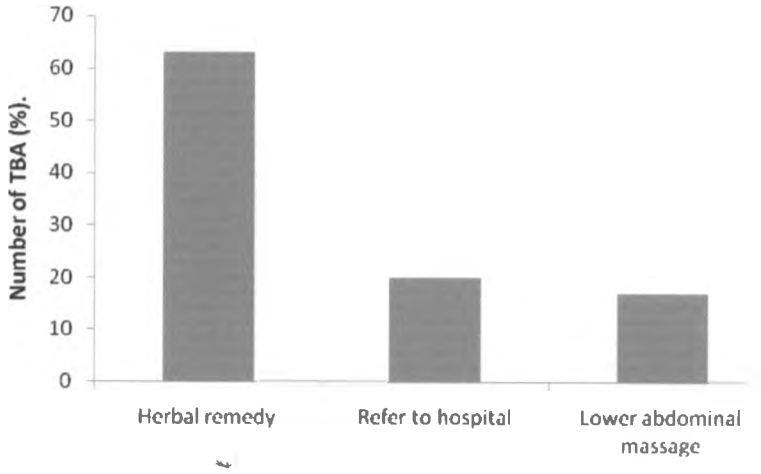



FIGURE 25: Interventions for the prevention of first trimester abortion.

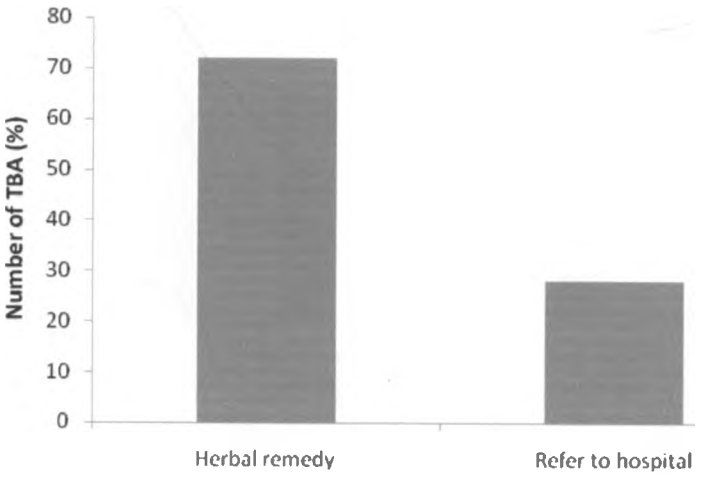



FIGURE 26: Interventions for the prevention of second and third trimester abortion.

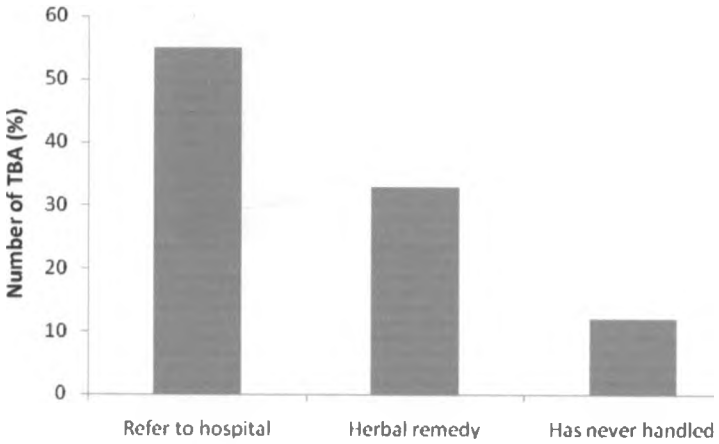



FIGURE 27: Interventions used by TBAs for the management of vomiting during pregnancy.

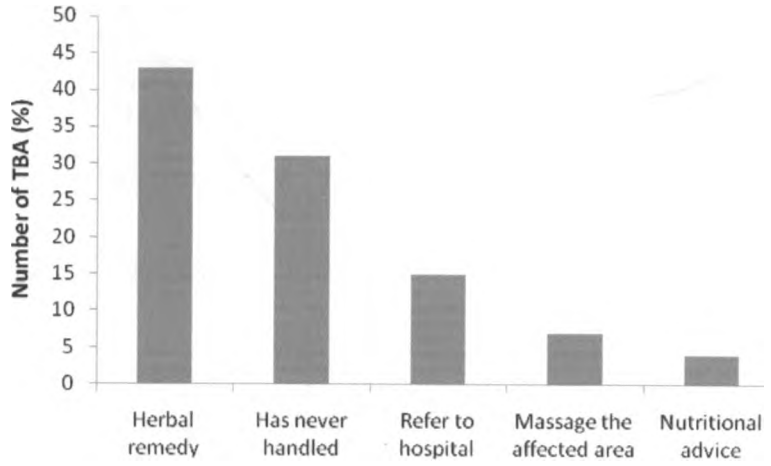



FIGURE 28: Interventions used by TBAs for the management of pregnancy edema.

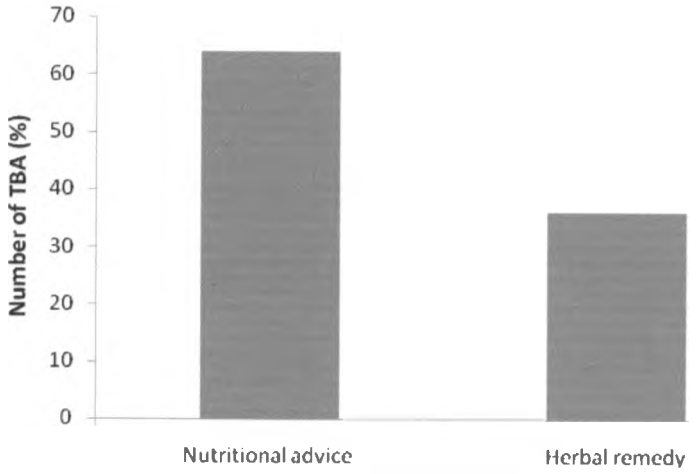



FIGURE 29: Interventions for the management of pregnancy anemia.

Table 1: Medicinal plants used to induce labor.

| BOTANICAL NAME | FAMILY NAME | LOCAL NAME | PLANT PART | ROUTE | DOSE |
|---|---|---|---|---|---|
| *Ricinus communis* | *Euphorbiaceae* | Mwaiki | R | O | 600 ml at once. |
| *Euclea divinorum* | *Ebenaceae* | Mukinyai | L | O | Clean root is chewed. |
| *Ocimum americana* | *Lamiaceae* | Mutaa | WP | O | 75 ml once |
| *Solanum incunum* | *Solanaceae* | Ngondu | R | O | 5g put in 300 ml water. |
| *Strychnos henningsii* | *Loganiaceae* | Muteta | L | O | 150 ml once |
| *Clausina anisettes* | *Retiree* | Muthiwa | L | O | 300 ml once |
| *Zanthoxylum chalybeum* | *Rutaceae* | Mukenea | R | O | Licking powder |
| *Sida tenuicarpa vollesen* | *Malvaceae* | Muemanzou | WP | O | 150ml × 2 daily |
| *Fragia brevipes* | *Euphorbiaceae* | Kinyeelya | R | O | Chew the root |

Key: O-Oral R-Root L-Leaves WP-Whole plant

Table 2: Medicinal plants used by TBAs for the management of protracted labor

| BOTANICAL NAME | FAMILY NAME | LOCAL NAME | PLANT PART | ROUTE | DOSAGE |
|---|---|---|---|---|---|
| *Ricinus communis* | *Euphorbiaceae* | Mwaiki | R | O | 300 ml at once. |
| *Euclea divinorum* | *Ebenaceae* | Mukinyai | L | O | Clean root is chewed. |
| *Acacia tortollis* | *Moraceae* | Mulaa | R | T | Apply on lower abdomen |
| *Ocinum americana* | *Labiatae* | Mutaa | L | O | 75 ml once |
| *Sida tenuicarpa vollesen* | *Malvaceae* | Muemanzou | WP | O | 150 ml twice a day |
| *Zanthoxylum chalybeum* | *Rutaceae* | Mukenea | R | O | Licks powder |
| *Fragia brevipes* | *Euphorbiaceae* | Kinyeelya | R | O | Chewing the root |
| *Steganotaenia araliacea* | *Apiaceae* | Muvuavui | L,S | O | 300 ml once |
| *Clausina anisatum* | *Rutaceae* | Muthiwa | L | O | 300 ml once |
| *Croton macrostachyus delile* | *Euphorbiaceae* | Mukondu | R | O | Chewing the root |

Key: O- oral, T- topical, R- root, ⊥-leaves, WP- whole plant, S- stem

Table 3: Medicinal plants used by TBAs for the management of post partum hemorrhage

| BOTANICAL NAME | FAMILY NAME | LOCAL NAME | PLANT PART | ROUTE | DOSAGE |
|---|---|---|---|---|---|
| *Ricinus communis* | *Euphorbiaceae* | Mwaiki | R | O | Chew young roots or 150 ml once |
| *Euclea divinorum* | *Ebenaceae* | Mukinyai | R | O | Clean the root then chew. |
| *Barleria eranthemoides* | *Acanthaceae* | Thangila | WP | T | Roast. Then powder is smeared |
| *Lippia javanica* | *Verbenaceae* | Muthieti | R / S | T | Roast. Then powder is smeared |
| *Stychnos henningsii* | *Loganiaceae* | Muteta | L | T | Roast. Then powder is smeared |
| *Ocimum americana* | *Labiatae* | Mutaa | WP | O | 150 ml thrice daily |
| *Fagaropsis hildebrandtii* | *Rutaceae* | Muvindavindi | R | O | 150 ml thrice daily for 7 days |
| *Croton macrostachyus delile* | *Euphorbiaceae* | Mukandu | L | O | 300 ml thrice daily for one week |
| *Pappea capensis* | *Sapindaceae* | Muva | B | O | 300 ml thrice daily for one week |
| *Aspilia mossambicensis* | *Compositae* | Muti | L | O | 150 ml daily for 3 days |
| *Hoslundia opposite vahl* | *Lamiaceae* | Musovi | L | O | 150 ml daily for 3 days |

| | | | | | |
|---|---|---|---|---|---|
| *Fuerstia africana* | *Labiatae* | Kalaku | L | O | 150 ml daily for 3 days |
| *Bidens pilosa* | *Compositae* | Munzee | WP | O | 150 ml daily for 3 days |
| *Vernona glabra vatke* | *Compositae* | Musavuni | L | O | 150 ml thrice daily for 2 days |
| *Clausina anisatum* | *Rutaceae* | Muthiwa | R | O | 300 ml thrice daily |

Key: O- oral T- topical WP- whole plant R- root S- stem L- leave B- bark

Table 4: Medicinal plants used by TBAs for the management of retained afterbirth

| BOTANICAL NAME | FAMILY NAME | LOCAL NAME | PLANT PART | ROUTE | DOSAGE |
|---|---|---|---|---|---|
| *Ricinus communis* | *Euphorbiaceae* | Mwaiki | R | O | 300 ml once |
| *Euclea divinorum* | *Ebenaceae* | Mukinyai | R | O | Root chewing or 75 ml drank. |
| *Withania somnifera* | *Solanaceae* | Mwianzo | L | O | 300ml once |
| *Bosia angustiafolia* | *Cupressaceae* | Mwenzenze | S | O | 150 ml once |
| *Aloe sceundiflora* | *Aloaceae* | Kiluma | S OR L | O | 150 ml once |
| *Clausina anisatum* | *Rutaceae* | Muthiwa | R | O | Chewing the roots |
| *Steganotaenia Araliaceae* | *Apiaceae* | Muvuavui | L or R | O | 75 ml once |

Key: O- oral L-leaves R- root S- stem

Table 5: Medicinal plants used by TBAs for the initiation of milk ejection

| Botanical name | Family name | Local name | Plant part | Route | Dosage |
|---|---|---|---|---|---|
| *Bidens pilosa* | *Compositae* | Munzee | WP | O | 300 ml three times daily for 3 days |
| *Carisa edulis* | *Apocynaceae* | Mukawa | R | O | 150 ml three times daily with meals |
| *Fagaropsis hildebrandtii* | *Rutaceae* | Muvindavindi | R | | |

Key: O- oral L- leaves WP- whole plant S- stem R- root

Table 6: Medicinal plants used by TBAs for the prevention of first trimester abortion

| BOTANICAL NAME | FAMILY NAME | LOCAL NAME | PLANT PART | ROUTE | DOSAGE |
|---|---|---|---|---|---|
| *Solanum incunum* | *Solanaceae* | Ngondu | L | T | 150 ml twice daily for 2 days |
| *Zanthoxylum chalybeum* | *Rutaceae* | Mukenea | R | O | |
| *Fagaropsis hildebrandtii* | *Rutaceae* | Muvindavindi | R | O | |
| *Carisa edulis* | *Apocynaceae* | Mukawa | R | O | |
| *Vernomia brachycalyx* | *Compositae* | Mukutu | R | O | 150 ml three times for 3 days |
| *Strychnos henningsii* | *Loganiaceae* | Muteta | L | O | 20 ml twice for 7 days |
| *Hoslundia opposite* | *Lamiaceae* | Musovi | L | | |
| *Bosia angustiafolia* | *Capparaceae* | Mwenzenze | L | | |
| *Ocimum americana* | *Labiatae* | Mutaa | WP | O | 150 ml three times for 7 days |
| *Stryranthes fruticosa* | | Muvinga | R | O | |
| *Hoslundia opposita* | *Labiatae* | Musovi | L | O | |
| *Amaranthus graecizans* | *Amaranthaceae* | Vuyaa | WP | O | 300 ml three times daily for 3 days |
| *Eulophia petersii rechs* | *Orchidaceae* | Kiongoa | R | O | |
| *Vernomia lasiopus* | *Compositae* | Muvatha | R | O | |
| *Bidens pilosa* | *Compositae* | Munzee | WP | O | 300 ml three times daily for 3 days |
| *Aspilia mossambicensis* | *Compositae* | Muti | L | O | |
| *Fuerstia africana* | *Labiatae* | Kalaku | L | O | |
| *Strychnos henningsii* | *Loganiaceae* | Kamuteta | L | O | 150 ml thrice for 3 days |
| *Sesanum angustiafolia* | *Pedaliaceae* | Luta | L | O | |

| | | | | | |
|---|---|---|---|---|---|
| *Sphaeranthus bullatus* | *Compositae* | Musonzoiya | L | O | 300 ml thrice for two days |
| *Vernomia glabra vatke* | *Compositae* | Musavuni | WP | O | |
| Ficus thonningii brume | Moraceae | Kiumo | S | T | Tied over the abdomen |
| Hydnora abyssinica | Hydnoraceae | Kimela | R | O | 5g in 300 ml water for three days |

Key: O- oral T- topical R- root L- leaves S- stem WP- whole plant

Table 7: Medicinal plants used by TBAs for the prevention of second and third trimester abortion.

| BOTANICAL NAME | FAMILY NAME | LOCAL NAME | PLANT PART | ROUTE | DOSE |
|---|---|---|---|---|---|
| *Ocimum americana* | *Labiatae* | Mutaa | WP | T | Pounded. Add water. Wash body daily for 7 days |
| *Plectranthus Cylindraceus* | *Labiatae* | Kio | WP | T | |
| *Solanum incunum* | *Solanaceae* | Ngondu | WP | T | |
| *Usnea usneoides* | *Parmeliaceae* | Mwii waivia | R | O | 300 ml thrice for 7 days |
| *Vernomia brachycalyx* | *Compositae* | Mukutu | R | O | |
| *Carisa edulis* | *Apocynaceae* | Mukawa | R | O | |
| *Terminalia brownie* | *Combretaceae* | Muuku | R | O | 150 ml twice for 2 days |
| *Kleinia squirosa* | *Asteraceae* | Kingendya-thenge | S | O | |
| *Asparagus buchanannii* | *Asparagaceae* | U,usya | S | O | |
| *Cynodon dactylon* | *Poaceae* | Ikoka grass | G | T | Tied over abdomen |
| *Vernomia lasiopus* | *Compositae* | Muvatha | R | O | 300 ml thrice for 3 days |
| *Aspilia mossambicensis* | *Compositae* | Muti | R | O | 300 ml thrice for 3 days |
| *Strychnos henningsii* | *Loganiaceae* | Muteta | L | O | 20 ml twice for 7 days |
| *Fagaropsis hildebrandtii* | *Rutaceae* | Muvindavindi | R | O | 150 ml twice a day |
| *Hydnora abyssinica* | *Hydnoraceae* | Kimela | R | O | 15g per day for 2 days |
| *Sphaeranthus bullatus* | *Compositae* | Musonzoiya | R | O | 300 ml thrice for 2 days |
| *Plectranthus barbatus* | *Lamiaceae* | Muvou | L | O | 300 ml daily for 2 days |

| | | | | | |
|---|---|---|---|---|---|
| *Aloe sceundiflora* | *Aloaceae* | Kiluma | R | O | 10 ml thrice for 7 days |
| *Sesamum angustifolium* | *Pedaliaceae* | Luta | R | O | 150 ml thrice for 3 days |
| Asparagus buchanannii | Liliaceae | U'usya | L | O | |
| Vernonia glabra vatke | Compositae | Musavuni | R | O | 300 ml thrice for 2 days |
| Ficus thonningii brume | Moraceae | Muumo | L | T | Tied over the abdomen for one week |
| Bidens pilosa | Compositae | Munzee | L | O | 150 ml thrice for 3 days |
| Fuerstia africana | Labiatae | Kalaku | R | O | |
| Hoslundia opposite vahl | Labiatae | Musovi | R | O | |

Key T- topical O- oral WP- whole plant S-stem G- grass R- root L-leaves

Table 8: Medicinal plants used by TBAs for the management of vomiting during pregnancy

| BOTANICAL NAME | FAMILY NAME | LOCAL NAME | PLANT PART | ROUTE | DOSAGE |
|---|---|---|---|---|---|
| *Rhus natalensis kraus* | *Anacardiaceae* | Mutheu | R | N | Lick and sniff powder |
| *Pentads parvifolia* | *Rubiaceae* | Kamumeti | R | N | Lick and sniff powder |
| *Zanthoxylum chalybeum* | *Rubiaceae* | Mukenea | L | O | 150 ml twice for 2 days |
| *Terminalia brownie* | *Combretaceae* | Muuku | L | O | 300 ml thrice daily |
| *Ocimum americana* | *Labiatae* | Mutaa | WP | O | |
| *Strychnos henningsii* | *Loganiaceae* | Muteta | L | O | 300 ml once |
| *Vernomia brachycalyx* | *Compositae* | Mukutu | R | O | |
| *Barleria erathemoides* | *Acanthaceae* | Thangila | WP | O | 10 ml thrice for 7 days |
| *Solanum incunum* | *Solanaceae* | Ngondu | L | O | 150 ml twice for 2 days |
| *Fagaropsis hildebrandtii* | *Rutaceae* | Muvindavindi | R | O | |
| *Carisa edulis* | *Apocynaceae* | Mukawa | R | O | |
| *Usnea usneoides* | *Parmeliaceae* | Mwii wavia | R | O | |
| *Boscia angustifolia* | *Capparacae* | Mwenzenze | L | O | |
| *Securing virosa* | *Euphorbiaceae* | Mukuulu | R | O | 20 ml thrice for 7 days |
| *Leonotis nepotifolia* | *Labiatae* | Mulo | R | O | 150 ml twice a day |
| *Vernomia lasiopus* | *Compositae* | Muvatha | R | O | 150 ml thrice for 3 days |
| *Rumex usambarensis* | *Polygonaceae* | Kyuvi | R | O | 5ml of mixture put in drinks |

| | | | | | |
|---|---|---|---|---|---|
| *Sesamum angustifolium* | *Pedaliaceae* | Luta | L | O | 150 ml thrice for 3 days |
| *Aloe sceundiflora* | *Aloaceae* | Kiluma | S | O | 10g twice a day |
| *Euphobia scheffleri* | *Euphobiaceae* | Kilembwa | S | O | Lick the powder |
| *Barleria erathemoides* | *Acanthaceae* | Thangila | WP | O | 5g powder in milk three times for 2 days |
| *Aspilia mossambicensis* | *Compositae* | Muti | WP | O | |
| *Hoslundia opposite* | *Lamiaceae* | Musovi | WP | O | |
| *Cynodon dactylon* | *Poaceae* | Ikoka grass | WP | T | Tied around neck one week |
| *Sphaeranthus bullatus* | *Compositae* | Musonzoiya | R | O | 300 ml daily for 3 days |
| *Plectranthus barbatus* | *Lamiaceae* | Muvou | R | O | |
| *Lannea schweinfurthii* | *Anacardiaceae* | Kithoona | R | O | 300 ml once |

Key: O- oral, N- nasal, T- topical, L- leaves, R- root, S- stem, WP- whole plant.

Table 9: Medicinal plants used by TBAs for the treatment of pregnancy edema

| BOTANICAL | FAMILY | LOCAL | PLANT PART | ROUTE | DOSAGE |
|---|---|---|---|---|---|
| *Zanha africana* | *Sapindaceae* | Mukolekya | R | O | 15g mixed with 300 ml water. Taken once |
| *Strychnos henningsii* | *Loganiaceae* | Muteta | L | O | 300 ml daily for 7 days |
| *Fuerstia africana* | *Labiatae* | Kalaku | WP | O | |
| *Erythrina abyssinica* | *Fabaceae* | Kivuti | L | O | |
| *Ficus sur* | *Moraceae* | Mukuyu | B | O | |
| *Ocimum americana* | *Leguminosae* | Mutaa | WP | O | 300 ml thrice daily for 2 weeks |
| *Strysanthes fruticosa* | *Pepllionae* | Muvinga | L | O | |
| *Sida tenuicarpa vollesen* | *Malvaceae* | Muem anzou | WP | O | 300 ml thrice for 3 days |
| *Zanthoxylum chalybeum* | *Rutaceae* | Mukenea | R | O | 150 ml thrice for 3 days |
| *Acacia nilotica* | *Fabaceae* | Musemei | B | O | 5g mixed with 1200 ml water, for 3 days |
| *Terminalia brownie* | *Combretaceae* | Muuku | S | O | |
| *Asparagus buchanannii* | *Asparagaceae* | U'usya | R | O | |
| *Kleinia squirosa* | *Asteraceae* | Kingendya-thenge | S | O | |
| *Plectranthus cylindraceus* | *Labiatae* | Kio | WP | O | |
| *Sphaeranthus bullatus* | *Composiate* | Musonzoiya | L | O | 300 ml thrice for 2 days |
| *Sesamum angustifolium* | *Pedaliaceae* | Luta | L | O | |
| *Oxygonum sinuatum* | *Polygonaceae* | Songee | L | O | 150 ml twice a day |
| *Clausina anisatum* | *Rutaceae* | Muthiwa | R | O | |
| *Dychoriste radicaus* | *Acanthaceae* | Kaila wimbu | R | O | 10g in 300 ml water. Taken once |
| *Helichrysum* | *Composiate* | Kilavyutia | R | O | |

| | | | | | |
|---|---|---|---|---|---|
| *glumaceum* | | | | | |
| *Cuscuta kilimanjari oliv* | *Convovulaceae* | Kawamama | B | O | |
| *Aspilia mossambicensis* | *Composiate* | Muti | B | O | 150 ml once |

Key: O- oral, B- bark, WP- whole plant, L-leaves, R- root, S-stem.

Table 10: Medicinal plants used by TBAs for the management of pregnancy anemia

| BOTANICAL | FAMILY | LOCAL NAME | PLANT PART | ROUTE | DOSAGE |
|---|---|---|---|---|---|
| *Terminalia brownie* | *Combretaceae* | Muuku | B | O | 300 ml twice a day |
| *Erythrina abyssinica* | *Fabaceae* | Muvuti | B | O | |
| *Fuerstia africana* | *Labiatae* | Kalaku | WP | O | |
| *Strychnos henningsii* | *Loganiaceae* | Muteta | L | O | |
| *Fagaropsis hildebrandtii* | *Rutaceae* | Muvindavindi | R | O | 150 ml twice |
| *Sesamum angustifolium* | *Pedaliaceae* | Luta | L | O | 300 ml once |
| *Lannea schweinfurthii* | *Anacardiacea* | kithoona | B | O | 10g added to porridge daily |

Key: O- oral, B- bark, L- leaves WP- whole plant.

Table 11: Examples of medicinal plants administered orally to pregnant women for durations of one to two weeks.

| BOTANICAL NAME | LOCAL NAME | PLANT PART | ROUTE | DOSAGE | CONDITION TREATED |
|---|---|---|---|---|---|
| *Clausina anisatum* | Muthiwa | R | O | 300ml daily for 3 days | PPH |
| *Ficus sur* | Mukuyu | B | O | 300ml daily for 7 days | edema |
| *Barleria erathemoides* | Thangila | WP | O | 10ml thrice for 7 days | vomiting |
| *Strychnos henningsii* | Muteta | L | O | 20ml twice for 7 days | abortion |
| *Ocimum americana* | Mutaa | WP | O | 150 ml thrice for 7 days | abortion |
| *Strysanthes fruticosa* | Muvinga | L | O | 300ml thrice for 2 weeks | edema |

Key: O-Oral, WP- whole plant, L- leaf, B- bark, R- root, PPH-post partum hemorrhage

Table 12: Examples of medicinal plants applied topically to pregnant women for durations of one to seven days:

| BOTANICAL NAME | LOCAL NAME | PLANT PART | ROUTE | DOSAGE | CONDITION TREATED |
|---|---|---|---|---|---|
| Cynodon dactylon | Ikoka grass | WP | T | Tied around neck for one week | vomiting |
| Ocinum americana | Mutaa | WP | T | Pound, add water. Wash body daily for one week | Threatened abortion |
| Plectranthus cylindraceus | Kio | WP | T | | |
| Solanum incunum | Ngondu | WP | T | | |

Key: WP- whole plant T- topical

## 3.2 *IN VITRO* STUDIES

In general, the results of the study show that an isolated rabbit uterus from a previously oestrogenized animal is capable of spontaneous and near regular contractions when placed in the correct medium which in this case was de jalon solution. These are presented as tracings Figure 30, 31, 34, 37, 38, 41 and 44 (i) and labeled negative control pattern for all the tests.

### 3.2.1 Positive control

Figure 30 shows the effect of OXT in the presence of PGF2α. Figure 30 (i) is the negative control tracing showing almost regular contraction pattern for a period of 5 minutes in de jalon alone. Figure 30 (ii) shows the effect of adding OXT and PGF2a into the organ bath of a non pregnant uterine strip. The amplitude of uterine contraction before addition of OXT and PGF2α was 5.5 ± 0.04. Upon addition of 1ml of OXT and 0.5 ml of PGF 2α the amplitude of contraction increased to 8.0 ± 0.21. The percentage increase in amplitude was 45%. Figure 30 (iii) shows the effect of OXT and PGF2α on pregnant uterine strip. The percentage increase in amplitude in this case was 75%.

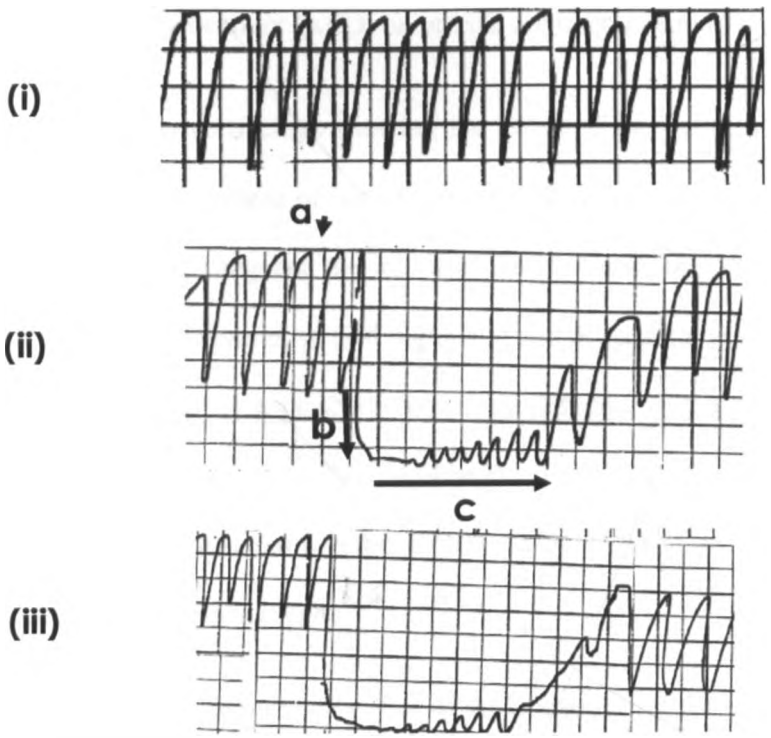



FIGURE 30: The effect of OXT and PGF 2α on uterine contraction pattern (positive control)

(i) Contraction pattern of negative control (de jalon alone)

(ii) Contraction pattern of non pregnant uterine strips

(iii) Contraction pattern of pregnant uterine strips

Key: **a**- point of infusion of OXT and PGF 2α **b**- increased amplitude (contraction strength). **c**- sustained contraction phase.

3.2.2 Effect of *Euclea divinorum* extracts

3.2.2.1 Effect of aqueous extract (AED) on uterine contraction strength

Only a few representative tracings showing the effect of the extracts are presented here as follows:- i) Contraction pattern of negative control, ii) contraction pattern at low doses (0.5 and 1.0 mg/ml) in non pregnant uterine strips in the absence of OXT and PGF 2α, iii) contraction pattern at medium dose (2.0 mg/ml) in non pregnant uterine strips in the presence of OXT and PGF 2α and iv) contraction pattern at high dose (4.0 mg/ml) in pregnant uterine strips in the presence of OXT and PGF 2α. The effect of 0.5 mg/ml and 1.0 mg/ml doses was similar and therefore considered together as low doses. All the tracings were however used for the statistical analysis and graphs.

Figure 31 (ii, iii and iv) shows the effect of AED extract on the uterine strips contraction pattern. Before addition of extract the amplitude of contraction was 8.0 ± 0.01 as shown in Figure 31 (i). Upon addition of AED extract, there was a strong initial contraction in all cases. The mean ± SEM amplitude of the initial contractions was 9.8 ± 0.05. The percentage increase in amplitude of contraction was 22.5%. In pregnant uterine strips in presence of OXT and PGF 2α; the AED extract had an augmenting effect on both the strength and frequency of contraction. The amplitude of uterine contraction was enhanced further at higher extract doses, (2.0 mg/ml) shown in Figure 31 (iii) and 4.0 mg/ml shown in Figure 31 (iv).

3.2.2.2 Effect of AED extract on contraction frequencies in non pregnant and pregnant uterus in the absence and presence of OXT and PGF 2α.

Before infusion of the extract the uterine contraction frequency in non pregnant uterine strips in the absence of OXT and PGF 2α was 1.343 ± 0.014. Following administration of the extract; the uteri exhibited strong contractions as shown in (Figure 31 ii).

Upon recovery the frequency of resumed contractions of non pregnant uterine strips varied with the extract dose as follows: The frequency of uterine contraction was 1.55 ± 0.029 at 0.5 mg/ml, 1.585 ± 0.03 at 1.0 mg/ml, 1.61 ± 0.016 at 2.0 mg/ml and 1.46 ± 0.053 at 4.0 mg/ml. The response was dose dependent, with highest frequency of uterine contraction exhibited at 2.0 mg/ml organ bath concentration. The mean ± SEM uterine contraction frequencies were higher in all treatments but not significantly different when compared to the negative control as shown in Figure 32 (i)

Figure 32 (ii) shows the effect of AED on non pregnant strips in the presence of OXT and PGF 2α. Before addition of extract and hormone, the mean ± SEM uterine contraction frequency was 1.605 ± 0.01. In the presence of extract, OXT and PGF 2α; the non pregnant uterine contraction frequency was 1.616 ± .005 at 0.5 mg/ml; 1.642 ± .0011 at 1.0 mg/ml; 1.686 ± 0.010 at 2.0 mg/ml and 1.81 ± 0.018 at 4.0 mg/ml. The mean ± SEM uterine contractions frequencies were significant ($P< 0.05$; $P< 0.01$) at 1.0, 2.0 and 4.0 mg/ml as illustrated in Figure 32 (ii).

The effect of AED extract on contraction frequencies of pregnant uterine strips in the absence of OXT and PGF $_{2\alpha}$ is given in Figure 32 (iii). During the negative control period (before addition of extract) the mean ± SEM uterine contraction frequency was 1.42 ± 0.448. Upon addition of extract, the pregnant uterine strip contraction frequency was 1.61± 0.374 at 0.5 mg/ml, 1.66 ± 0.476 at 1.0 mg/ml, 1.78 ± 0.504 at 2.0 mg/ml and 2.22 ± 0.494 at 4.0 mg/ml.

The mean ± SEM uterine contraction frequency was significant ($P< 0.05$ to $P< 0.01$) at 1.0, 2.0 and 4.0 mg/ml extracts concentrations as shown in Figure 32 (iii).

Figure 32 (iv) shows the effect of AED extract on contraction frequency of pregnant uterus in the presence of OXT and PGF 2α. Uterine contraction frequency before addition of extract and hormones was 9.12 ± 0.296. Upon addition of extracts, the uterotonic effect of AED was enhanced in the presence of OXT and PGF 2α. The uterine contraction frequency was 13.68 ± 0.536 at 0.5 mg/ml, 14.2 ± 0.906 at 1.0 mg/ml, 14.82 ± 0.753 at 2.0 mg/ml and 15.42 ± 0.937 at 4.0 mg/ml. The mean ± SEM contraction frequencies were significant ($P< 0.01$ to $P< 0.001$) at 0.5, 1.0, 2.0 and 4.0 mg/ml extract dose levels as shown in Figure 32 (iv).

### 3.2.2.3 Summary of the effect of aqueous (AED) extract on uterine strips

Figure 33 shows in summary, a comparison of the effects of AED extract on contraction frequencies of non pregnant and pregnant uterine strip in the presence and absence of OXT and PGF 2α. The effect of AED was significant at 1.0 to 4.0 mg/ml extract doses in non pregnant uterine strips in the presence of OXT and PGF 2α and in pregnant strips in the absence or presence of OXT and PGF 2α ($P< 0.05$ to $P< 0.001$). AED extract had the most significant effect in pregnant uterine tissue in the presence of OXT and PGF 2α. In this case the results were significant ($P< 0.01$ to $P< 0.001$) at all extract dose levels.

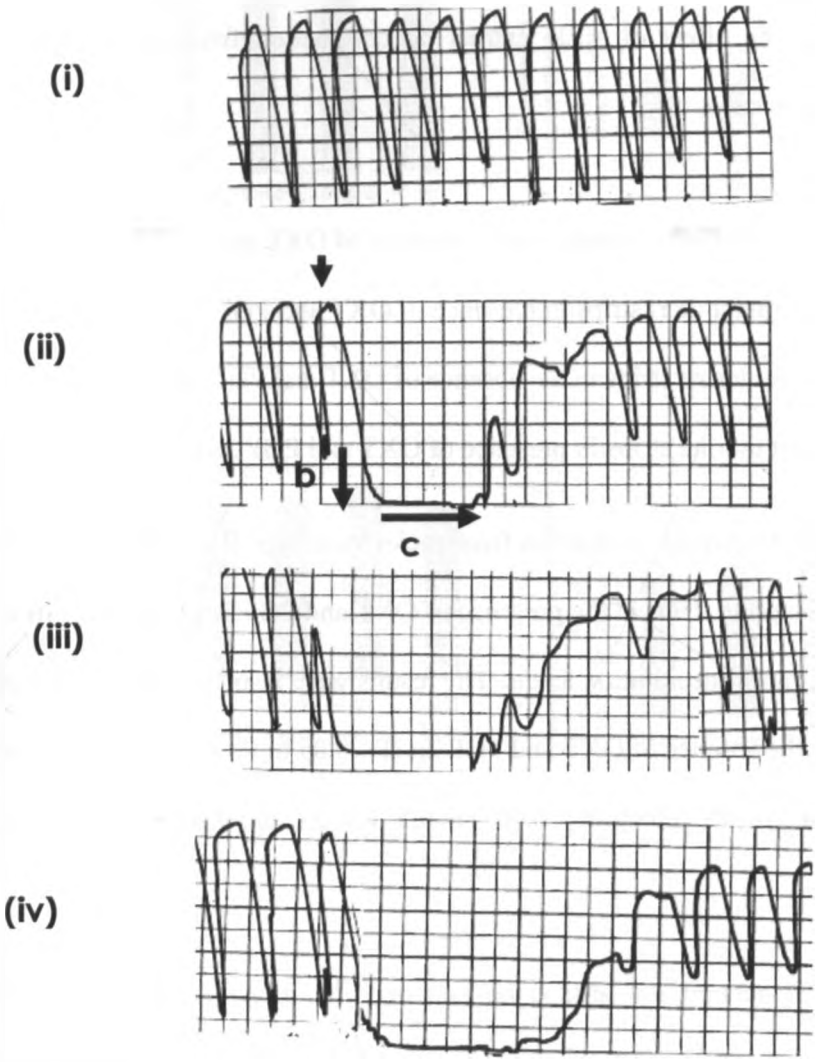



FIGURE 31: The effect of AED extract on contraction pattern of pregnant and non pregnan uterine strips

Key: **a**- point of extract infusion **b**- increased amplitude (contraction strength). **c**- sustained contraction phase.

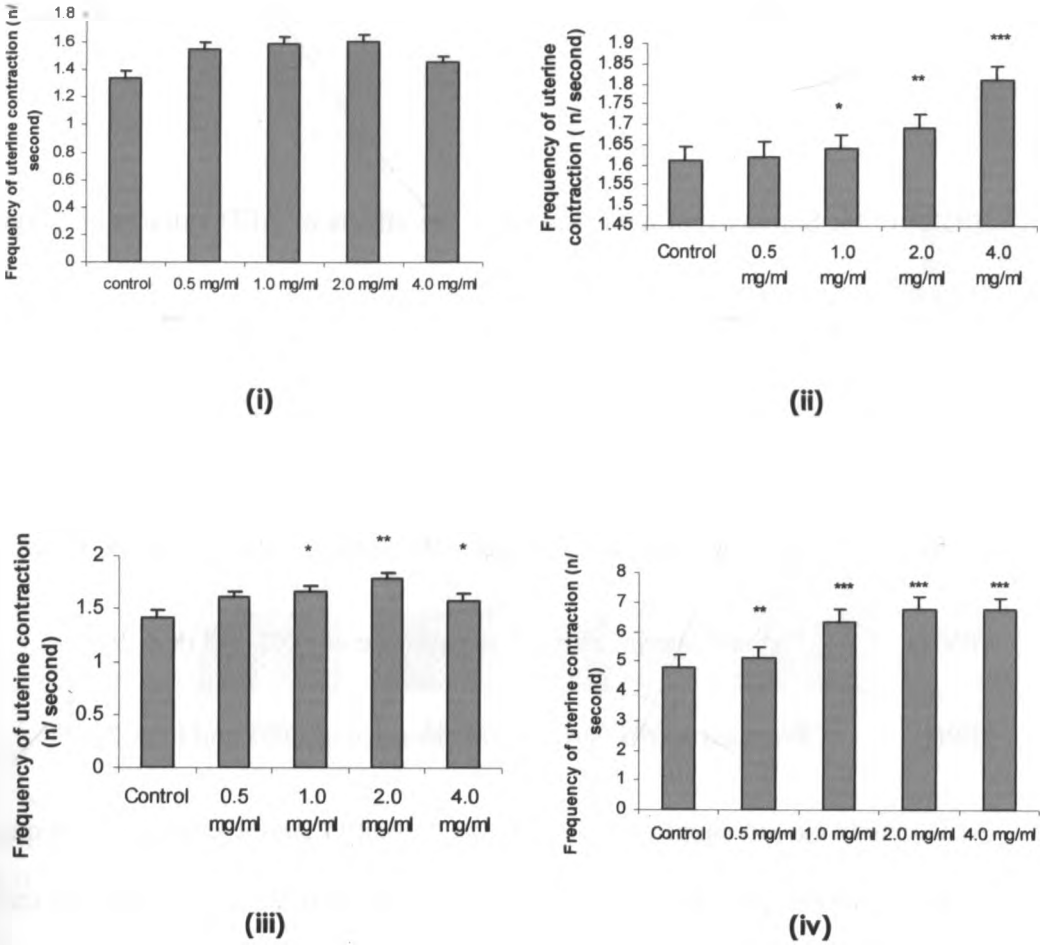



FIGURE 32: The effect of AED extract on contraction frequencies of pregnant and non pregnant uterine strips

* P< 0.05, ** P< 0.01, ***P < 0.001.

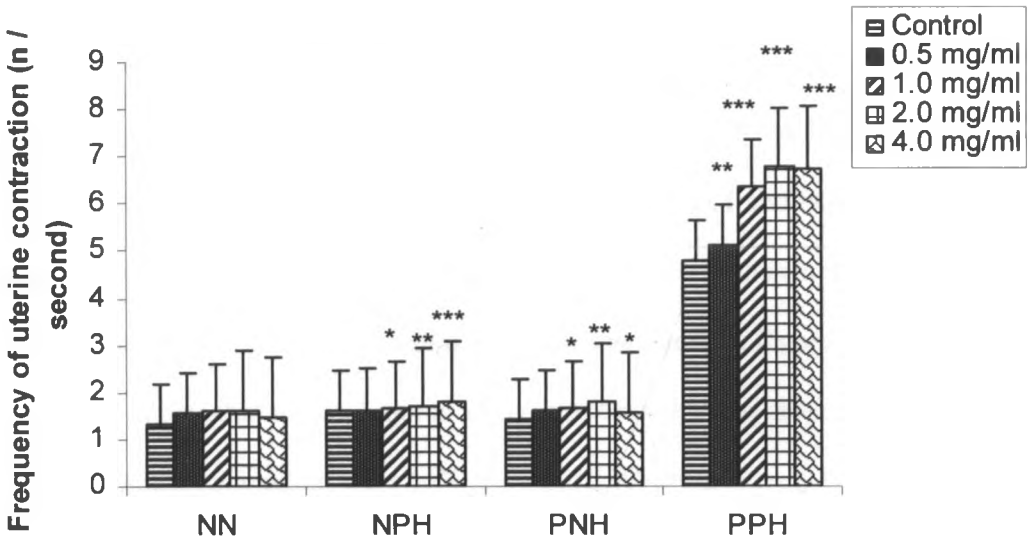



FIGURE 33: Summary of comparisons of the effects of AED extracts on pregnant and non pregnant uterine strips

*P< 0.05 ** P< 0.01 *** P< 0.001.

3.2.2.4 The effect of ethanol *Euclea divinorum* (EED) extract on contraction strength

Figure 34 shows the effect of EED on uterine strip contraction pattern in the presence and absence of OXT and PGF 2α. The mean ± SEM contraction amplitude before addition of extract was 4.5 ± 0.02. All extract doses caused an initial sharp contraction upon addition as indicated by an increase in the amplitude. The mean ± SEM increase in amplitudes of contraction was 6.5 ± 0.04 at 0.5 and 1.0 mg/ml in the absence of OXT and PGF 2α. in non pregnant uterus, Figure 34 (ii). In the presence of hormones however, the amplitude of contraction increased to 7.5 ± 0.02 at 2.0 mg/ml in non pregnant uterus, Figure 34 (iii) and 8.0 ± 0.01 at 4.0 mg/ml in pregnant uterus, Figures 34 (iv) respectively. The percentage increases in the amplitude of initial contraction were 44%, 36% and 100% respectively (Figure 34 ii, iii, and iv).

3.2.2.5 The effect of EED extract on contraction frequencies in non pregnant and pregnant uterine strips in the absence and presence of OXT and PGF 2α.

The results of contraction frequencies are given in Figure 35. The Mean ± SEM contraction frequency before addition of extract was 1.94 ± 0.28. Upon addition of extracts and following the strong initial contraction, the frequencies of resumed contractions were not significant when compared to negative control, Figure 35 (i). The mean ± SEM contraction frequencies were 2.36 ± 0.31, 2.53 ± 0.31, 2.7 ± 0.66 and 2.35 ± 0.53 at 0.5, 1.0, 2.0 and 4.0 mg/ml respectively as shown in Figure 35 (i).

Effect of EED extract on contraction frequencies in non pregnant uterine strips in the presence of OXT and PGF 2α is given in Figure 35 (ii). The mean ± SEM uterine contraction frequency during the negative control period was 2.71 ± 0.2. Upon addition of the extract, OXT and PGF 2α, the contractions frequencies were higher ranging from 3.22 ± 0.31, 3.80 ± 0.2, 4.13 ± 0.2, and 3.74 ± 0.2 at the respective dose levels (0.5 to 4.0 mg/ml). The frequencies were significant ($P < 0.05$) at 1.0 and 2.0 mg/ml as shown in Figure 35 (ii).

Figure 35 (iii) shows the effect of EED extract on contraction frequency in pregnant uterine strips in the absence of OXT and PGF 2α. The mean ± SEM contraction frequency during the negative control period was 2.16 ±0.14. Contraction frequencies of pregnant uterine strip were not significantly different at 0.5 (2.64 ± 0.1), 1.0 (3.39 ± 0.2) and 4.0 mg/ml (2.79 ± 0.1) dose levels. Significant response was observed only at 2.0 mg/ml (Figure 35 (iii). At this dose level the contraction frequency was (3.62 ± 0.13).

The effect of EED extract on contraction frequencies in pregnant uterine strips in the presence of OXT and PGF 2α is presented in Figure 35 (iv). The presence of OXT and PGF 2α augmented the effect of the extract on the pregnant uterine strips. The strip responded with increased contractions following the initial strong contraction. The contraction frequencies were 7.34 ± 0.19 at 1.0 mg/ml, 8.42 ± 0.26 at 2.0 mg/ml and 7.28 ± 0.26 at 4.0 mg/ml. The results were significant ($P< 0.01$, $P< 0.001$) at 1.0, 2.0 and 4.0 mg/ml respectively. ** $P < 0.01$, *** $P< 0.001$.

3.2.2.6 Summary of the effect of EED extract on uterine strips

Figure 36 shows a comparison of the effects of EED extract on contraction frequencies of pregnant and non pregnant uterine strip in summary. EED extract had no significant response

in non pregnant uterine strip in the absence of OXT and PGF 2α. However in non pregnant uterine strips in the presence of OXT and PGF 2α the results were significant ($P< 0.05$) at 1.0 and 2.0 mg/ml. In pregnant strips in the absence of hormones the results were significant only at 2.0mg/ml. The most significant response was observed with pregnant uterine strip in the presence of OXT and PGF2α at 1.0 mg/ml ($P< 0.01$), 2.0 mg/ml ($P< 0.001$) and 4.0 mg/ml ($P < 0.01$).

3.2.2.7 Effect of chloroform *Euclea divinorum* (CED) extract on pregnant and non pregnant uterine strips.

Upon addition of chloroform *Euclea divinorum* (CED) extract into the organ bath solution, the non pregnant uterine responded with a prolonged relaxation which lasted about 3 minutes. Upon recovery the resumed contractions were slower than negative control Figure 37 (ii and iii). The effect was similar on the pregnant uterine strip both in the presence and absence of OXT and PGF 2α Figure 37(iv). Upon recovery however, resumed contractions were similar to those exhibited during the negative control period.

FIGURE 34: The effect of EED extract on contraction pattern of pregnant and non preg uterine strips

(i) Contraction pattern of negative control (de jalon alone)

(ii) Contraction pattern of non pregnant uterine strips at low doses (0.5 and 1.0 mg/ml)

(iii) Contraction pattern of non pregnant uterine strips at medium dose (2.0 mg/ml) in presence of OXT and PGF 2α.

(iv) Contraction pattern of pregnant uterine strips at high dose (4.0 mg/ml) in the prese of OXT and PGF 2α.

All extract doses caused an initial sharp contraction of the uterine strip as indicated by an increase in the amplitude, Figure 34 (ii). The increase in amplitude of contraction was furt enhanced in the presence of OXT and PGF 2α, Figure 34 (iii and iv) in pregnant and non pregnant uterine strips.

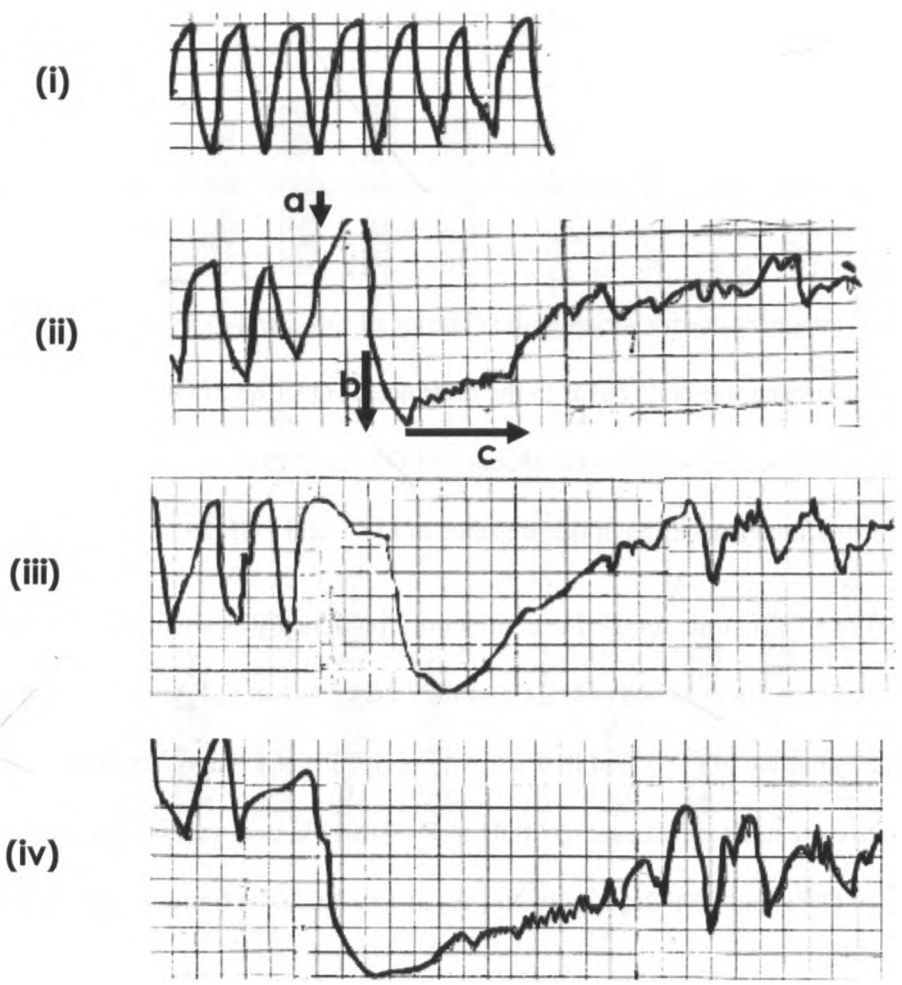



FIGURE 34: The effect of EED extract on contraction pattern of pregnant and non pregnant uterine strips

Key: **a**- point of extract infusion **b**- increased amplitude (contraction strength). **c**- sustained contraction phase.

FIGURE 35: The effects of EED extract on uterine contraction frequencies in pregnant non pregnant strips:

(i) Non pregnant uterine strips in the absence of OXT and PGF 2α.

(ii) Non pregnant uterine strips in the presence of OXT and PGF 2α

(iii)Pregnant uterine strips in the absence of OXT and PGF 2α.

(iv)Pregnant uterine strips in the presence of OXT and PGF 2α.

The effect of EED extract on uterine contraction frequency was significant ($P<0.05$) in non pregnant strips in the presence of OXT and PGF 2α as shown in Figure 35 (ii) and in pregn strips in the absence of OXT and PGF 2α, Figure 35 (iii) at 1.0 and 2.0 mg/ml dose levels. The results were most significant ($p< 0.01$ to $P< 0.001$) in pregnant uterine strips in the presence of OXT and PGF 2α, Figure 35 ( iv) at 1.0, 2.0 and 4.0 mg/ml extract dose levels.

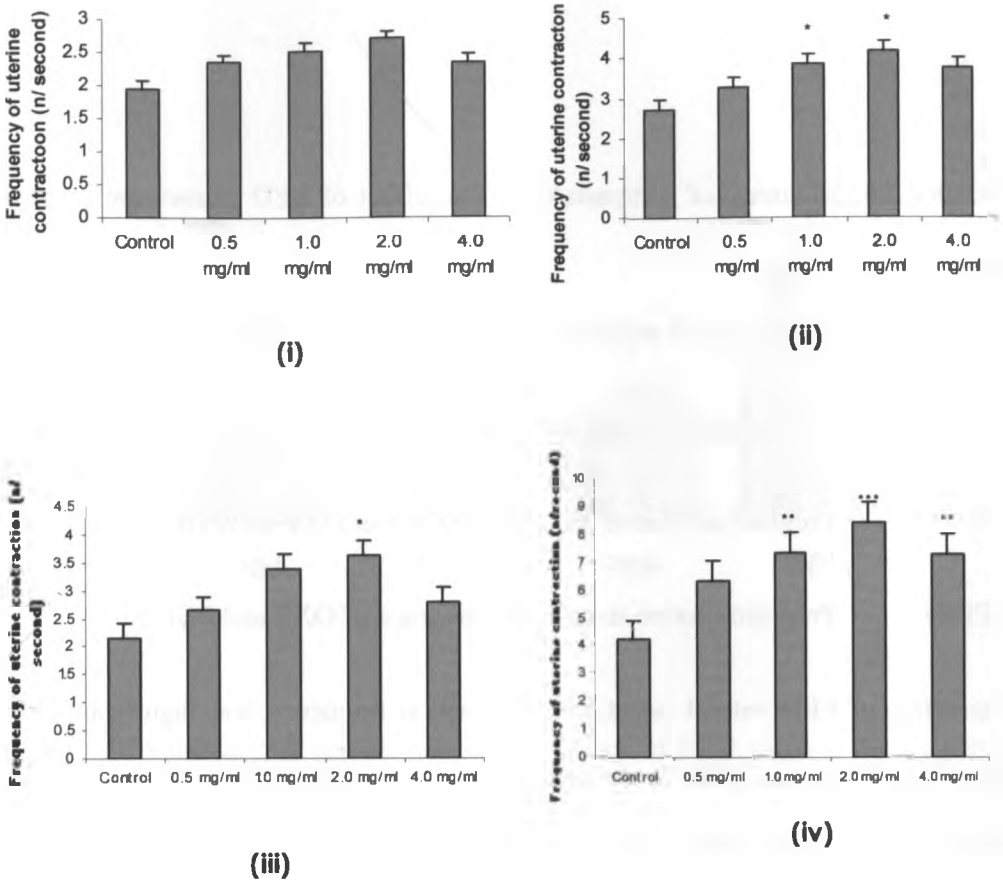



FIGURE 35: The effects of EED extract on uterine contraction frequencies in pregnant and non pregnant strips:

* P< 0.05, ** P< 0.01, ***P < 0.001.

FIGURE 36: Summary of comparisons of the effect of EED extracts on pregnant and pregnant uterine strips.

(NN) Non pregnant uterine strips in the absence of OXT and PGF 2α

(NPH) Non pregnant uterine strips in the presence of OXT and PGF 2α

(PNH) Pregnant uterine strips in the absence of OXT and PGF 2α

(PPH) Pregnant uterine strips in the presence of OXT and PGF 2α

The effect of EED extract on uterine contraction frequency was significant ($P<0.05$ $0.01$) in non pregnant strips in the presence of OXT and PGF 2α and in pregnant strips absence of OXT and PGF 2α at 1.0 and 2.0 mg/ml dose levels. The results were significant ($p< 0.01$ to $P< 0.001$) in pregnant uterine strips in the presence of OXT and 2α at 1.0, 2.0 and 4.0 mg/ml extract dose levels

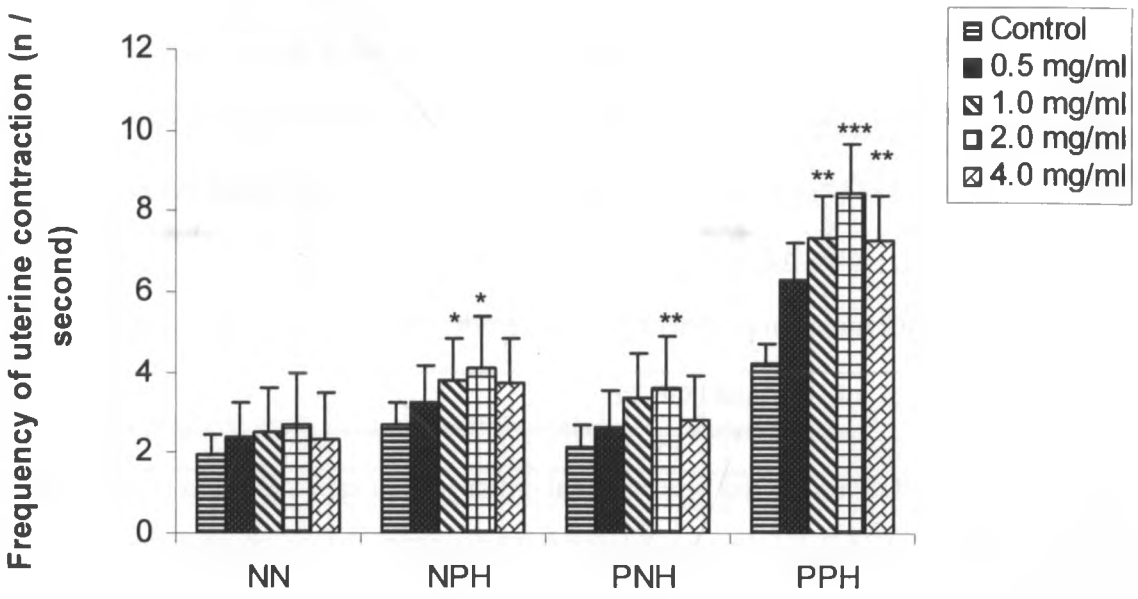



FIGURE 36: Summary of comparisons of the effect of EED extracts on pregnant and non pregnant uterine strips.

*P < 0.05; ** P < 0.01, ***P< 0.001

FIGURE 37: The effect of CED extract on contraction pattern of pregnant and no
uterine strips

(i) Contraction pattern of negative control (de jalon alone)

(ii) Contraction pattern of non pregnant uterine strips at low doses (0.5 and 1.0 m

(iii) Contraction pattern of non pregnant uterine strips at medium dose (2.0 mg/m
presence of OXT and PGF 2α.

(iv)Contraction pattern of pregnant uterine strips at high dose (4.0 mg/ml) in the
of OXT and PGF 2α.

The CED extract effect was an initial prolonged relaxation phase in both the non pre
pregnant uterine strips in the absence and presence of OXT and PGF 2α, Figure 37 (
iv).

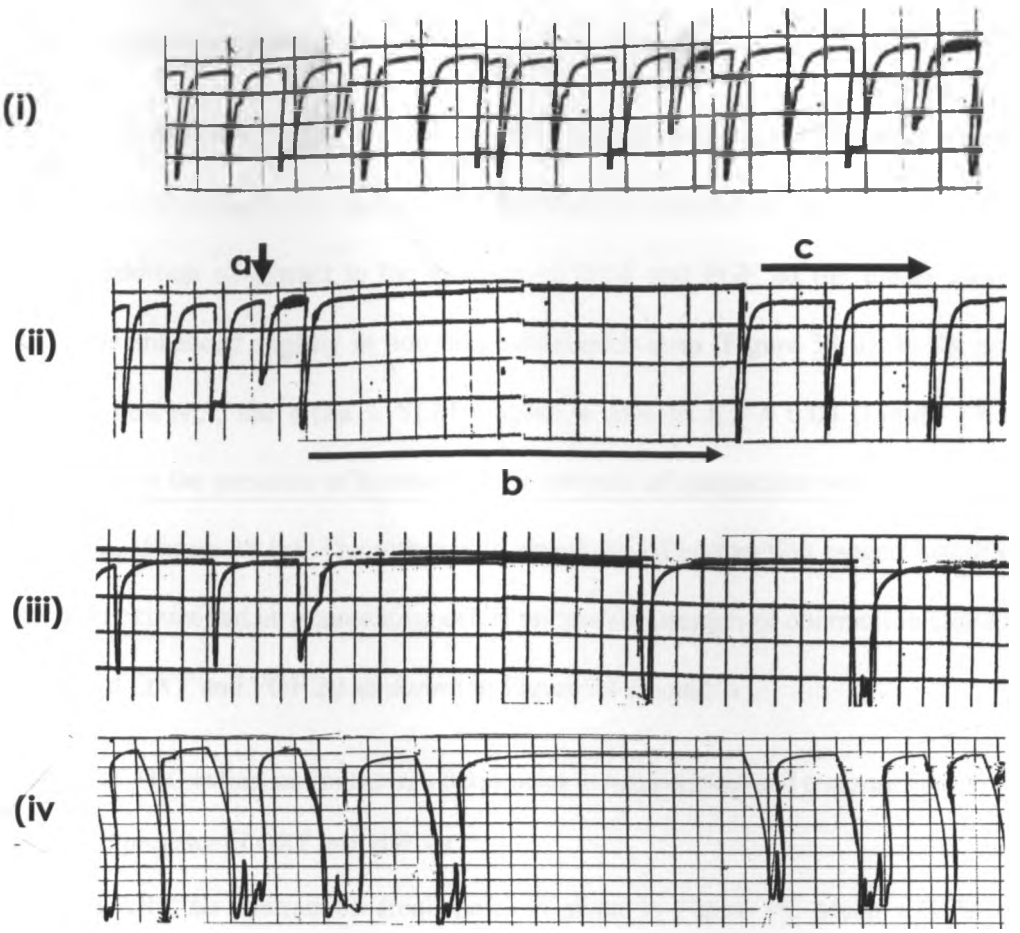



FIGURE 37: The effect of CED extract on contraction pattern of pregnant and non pregnant uterine strips

Key: **a**- point of extract infusion **b**- sustained relaxation phase **c**- resumed contractions.

### 3.2.3 Effect of *Ricinus communis* extracts

#### 3.2.3.1 Effect of aqueous *Ricinus communis* (ARC) extract on uterine contraction strength.

Before addition of extracts or hormones the amplitude of contraction was 5.5 ± 0.01 (Figure 38 i). Upon addition of extract in the absence of OXT and PGF 2α the initial contraction amplitude was enhanced slightly in non pregnant uterine strip (Figure 38 ii). In the presence of hormones however, the mean ± SEM amplitude rose to 8.5 ± 0.04 (Figure 38 iii). In pregnant uterus in the presence of hormone the amplitude of contraction was further enhanced to 10.5 ± 0.02. (Figure 38 iv). The increase in amplitude of contraction ranged between 55% and 60%. The extract had an augmenting effect on uterine strength of contraction especially in the presence of OXT and PGF 2α as shown in Figure 38 (iii and iv).

#### 3.2.3.2 Effect of ARC extract on contraction frequencies in non pregnant and pregnant uterine strips in the absence and presence of OXT and PGF 2α

The effect of ARC on contraction frequencies is given in Figure 39. Mean ± SEM uterine contraction frequency before addition of extract was 1.86 ± 0.342. Following the initial strong contraction the mean ± SEM frequency of resumed contractions varied with the extract dose as follows; 2.1 ± 0.41 at 0.5 mg/ml, 2.34 ± 0.497 at 1.0 mg/ml, 2.61 ± 0.528 at 2.0 mg/ml and 2.24 ± 0.504 at 4.0 mg/ml. The results were significant ($P< 0.05$) at 1.0 and 2.0 mg/ml as shown in Figure 39 (i). The effect of ARC extract on non pregnant uterine strips in the presence of OXT and PGF 2α. show that before the extract was added, the mean ± SEM uterine contraction frequency was 5.04 ± 0.18. Upon addition of extract in the presence of OXT and PGF 2α; the mean ± SEM frequency of uterine contraction was 5.58 ± 0.136 at 0.5 mg/ml, 6.06 ± 0.116 at 1.0 mg/ml, 6.54 ± 0.117 at 2.0 mg/ml and 6.04 ± 0.157 at 4.0 mg /ml.

The results were significant ($P < 0.05$ to $P < 0.01$) at 1.0, 2.0 and 4.0 mg/ml as shown in Figure 39 (ii). The effect of ARC extract on pregnant uterine strips in the absence of OXT and PGF 2 α is shown in Figure 39 (iii). The mean ± SEM contraction frequency during the negative control period was 2.72 ± 0.41. Upon addition of extract the mean ± SEM contraction frequencies were 3.9 ± 0.51, 5.18 ± 0.59, 5.86 ± 0.44 and 5.36 ± 0.48 at 0.5, 1.0, 2.0 and 4.0 mg/ml respectively. The results were significant ($P< 0.05$ to $P< 0.01$) at 1.0, 2.0 and 4.0 mg/ml as shown in Figure 39 (iii).

Effect of ARC extract on pregnant uterine strips in the presence of OXT and PGF 2 α is given in Figure 39 (iv). The mean ± SEM contraction frequency during the negative control period was 4.58 ± 0.26. In the presence of OXT and PGF 2α the mean ± SEM contraction frequencies were enhanced as follows; 6.5 ± 0.49 at 0.5 mg/ml, 8.26 ± 0.42 at 1.0 mg/ml, 8.77 ± 0.47 at 2.0 mg/ml and 6.97 ± 0.65 at 4.0 mg /ml. The results were significant ($P < 0.01$, $P< 0.001$) at 1.0 mg/ml, 2.0 and 4.0 mg/ml in a dose dependent manner (Figure 39 iv).

3.2.3.3 Summary of the effect of aqueous (ARC) extract on uterine strips

Figure 40 shows a comparison of the effects of ARC extract on contraction frequencies of non pregnant and pregnant uterine strip in the presence and absence of OXT and PGF 2α. ARC extract had significant ($P< 0.05$) response in non pregnant uterine strip in the absence of hormone, in non pregnant uterine strip in the presence of OXT and PGF 2α, ($P< 0.05$ to $P < 0.01$), in pregnant uterine strip in the absence of OXT and PGF 2α ($P< 0.05$ to $P < 0.01$). The most significant response was observed in pregnant uterine strip in the presence of OXT and PGF 2α ( $P < 0.01$ to $P < 0.001$).

FIGURE 38: The effect of ARC extract on uterine contraction pattern in pregnant a
pregnant strips

(i) Contraction pattern of negative control (de jalon alone)

(ii) Contraction pattern of non pregnant uterine strips at low doses (0.5 and 1.0 mg/

(iii) Contraction pattern of non pregnant uterine strips at medium dose (2.0 mg/ml)
presence of OXT and PGF 2α.

(iv)Contraction pattern of pregnant uterine strips at high dose (4.0 mg/ml) in the pr
of OXT and PGF 2α.

The extract caused a slight contraction of the uterine strip as indicated by an increase
amplitude, Figure 38 (ii). In the presence of OXT and PGF 2α the amplitude of cont
increased, Figure 38 (iii). The extract had an augmenting effect on uterine stren
contraction especially in pregnant uterine strips in the presence of OXT and PGF 2α as
in Figure 38 (iii and iv).

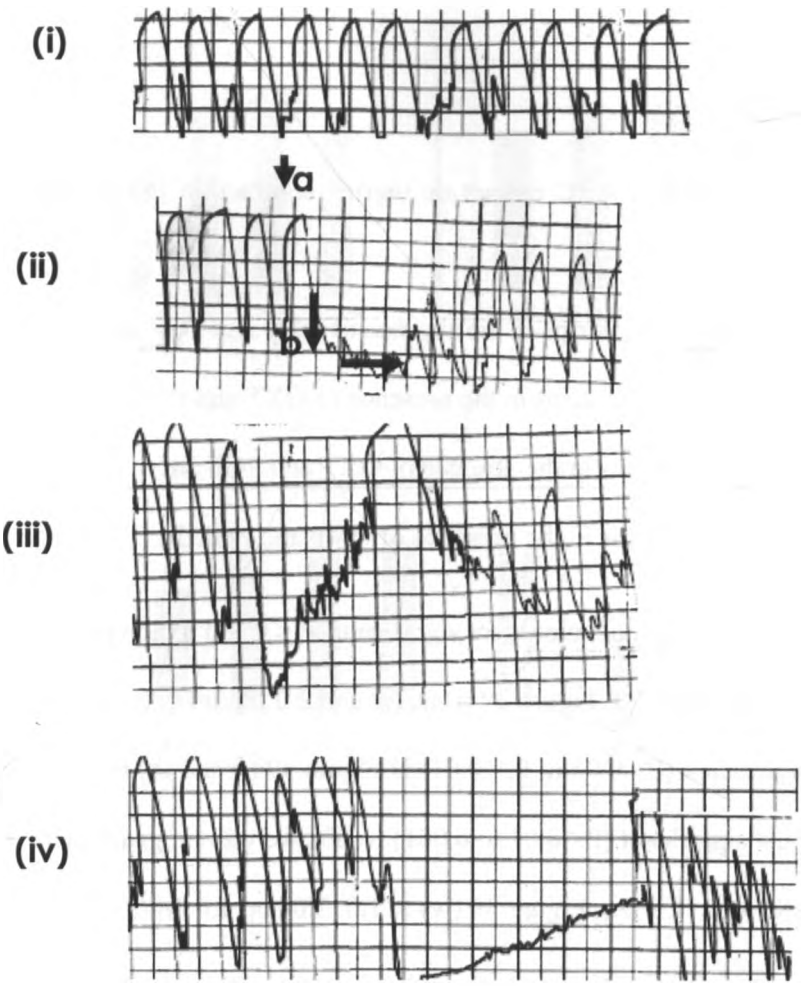



FIGURE 38: The effect of ARC extract on uterine contraction pattern in pregnant and non pregnant strips

Key: **a**- point of extract infusion **b**- sustained contraction phase **c**- resumed contractions.

FIGURE 39: The effect of ARC extract on uterine contraction frequencies in pregnant an non pregnant strips

(i) Non pregnant uterine strips in the absence of OXT and PGF 2α.

(ii) Non pregnant uterine strips in the presence of OXT and PGF 2α

(iii)Pregnant uterine strips in the absence of OXT and PGF 2α.

(iv) Pregnant uterine strips in the presence of OXT and PGF 2α.

The uterine contraction frequencies were significant ($P < 0.05$) in non pregnant strips in the absence of OXT and PGF 2α, Figure 39 (i) at 1.0 and 2.0 mg/ml extract dose levels. The results were significant ($P< 0.05$ to $P < 0.01$) in Figure 39 (ii and iii) at 1.0, 2.0 and 4.0 mg/ml. The most significant ($P< 0.01$ to 0.001) results were in pregnant uterine strips in the presence of OXT and PGF 2α, Figure 39 (iv) at 1.0, 2.0 and 4.0 mg/ml.

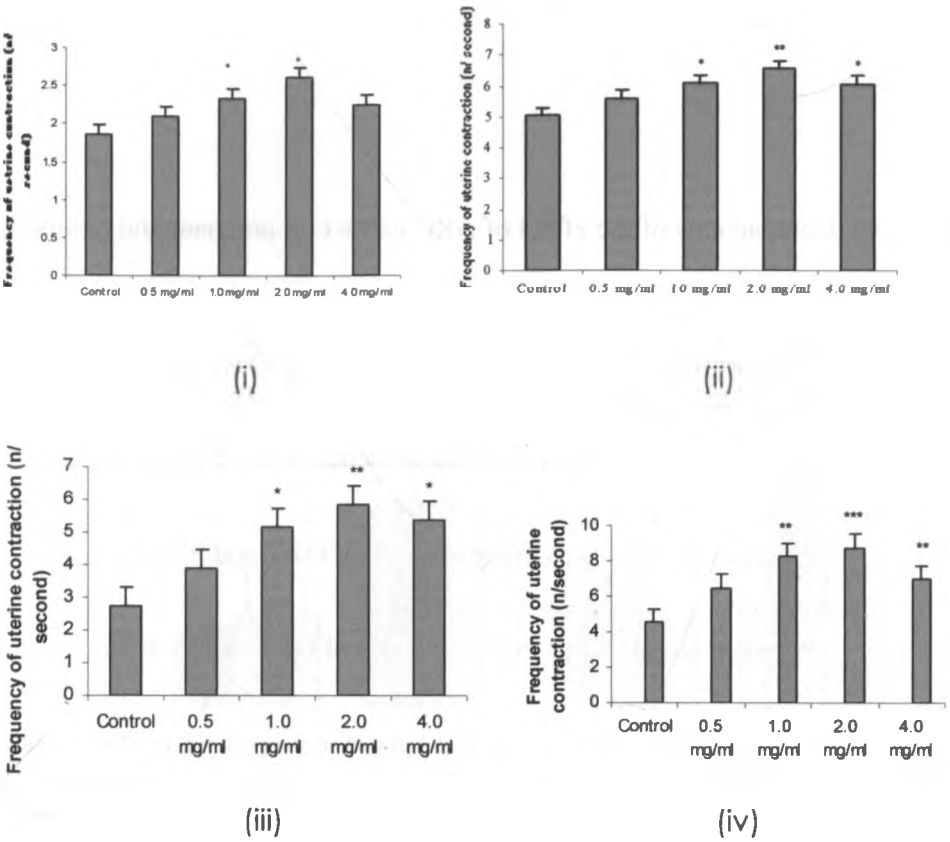



FIGURE 39: The effect of ARC extract on uterine contraction frequencies in pregnant and non pregnant strips

(i) Non pregnant uterine strips in the absence of OXT and PGF 2α.

(ii) Non pregnant uterine strips in the presence of OXT and PGF 2α

(iii)Pregnant uterine strips in the absence of OXT and PGF 2α.

(iv) Pregnant uterine strips in the presence of OXT and PGF 2α.

* P< 0.05, ** P< 0.01, ***P < 0.001.

FIGURE 40: Comparisons of the effect of ARC extract on pregnant and non pregnant uterine strips

(NN) Non pregnant uterine strips in the absence of OXT and PGF 2α

(NPH) Non pregnant uterine strips in the presence of OXT and PGF 2α

(PNH) Pregnant uterine strips in the absence of OXT and PGF 2α

(PPH) Pregnant uterine strips in the presence of OXT and PGF 2α

The results were significant ($P< 0.05$) in non pregnant uterine strips in the absence of OXT and PGF 2α at 1.0 and 2.0 mg/ml extract dose level. In non pregnant uterine strips in the presence of OXT and PGF 2α and in pregnant strips in the absence of OXT and PGF 2α the results were significant ($P< 0.05$ to $P< 0.01$) at 1.0, 2.0 and 4.0 mg/ml extract concentration levels. The most significant ($P< 0.01$ to $P< 0.001$) results were however observed in pregnant uterine strips in the presence of OXT and PGF 2α at 1.0, 2.0 and 4.0 mg/ml extract concentration levels.

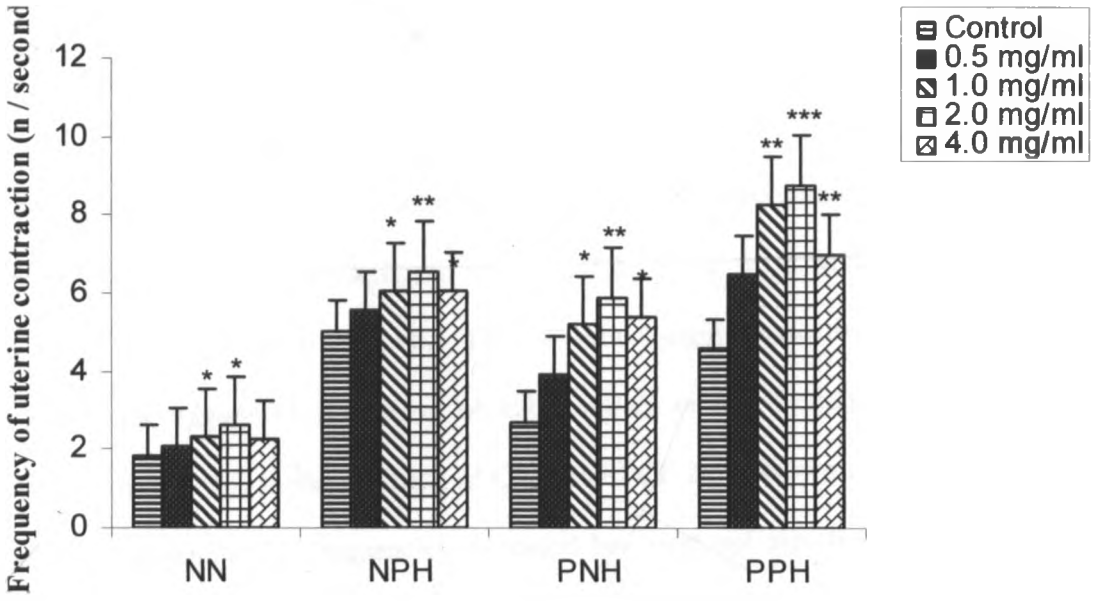



FIGURE 40: Comparisons of the effect of ARC extract on pregnant and non pregnant uterine strips

(NN) Non pregnant uterine strips in the absence of OXT and PGF 2α

(NPH) Non pregnant uterine strips in the presence of OXT and PGF 2α

(PNH) Pregnant uterine strips in the absence of OXT and PGF 2α

(PPH) Pregnant uterine strips in the presence of OXT and PGF 2α

( P<0.001). * P<0.05 ** P< 0.01 *** P< 0.001.

3.2.3.4 Effect of ethanol *Ricinus communis* (ERC) extract on uterine contraction strength

ERC extract had no significant effect on the strength of contractions of either non pregnant or pregnant uterine strips (Figure 40).

3.2.3.5 Effect of ERC extract on contraction frequencies in non pregnant and pregnant uterine strips in the absence and presence of OXT and PGF 2α.

The mean ± SEM frequency of contraction during the negative control period was 2.18 ± 0.23. The frequencies of contraction in non pregnant uterine strips were 2.8 ± 0.41, 3.24 ± 0.26, 2.93 ± 0.41 and 2.26 ± 0.52 at 0.5, 1.0, 2.0 and 4.0 mg/ml respectively. The results were not significant, Figure 41 (i). Effect of ERC extract on contraction frequencies in non pregnant uterine strips in the presence of OXT and PGF 2α is shown in Figure 41 (ii). The mean ± SEM contraction frequencies increased but were not significantly different when compared to the control (3.6 ± 0.18). The contraction frequencies here were 3.89 ± 0.25; 4.57 ± 0.32; 4.35 ± 0.3 and 3.81 ± 0.26 at 0.5, 1.0, 2.0 and 4.0 mg/ml respectively. The effect of ERC extract on contraction frequencies in pregnant uterine strips in the absence of OXT and PGF 2α.is shown in Figure 41 (iii). The contraction frequencies were 3.77± 0.17 at 0.5 mg/ml, 4.1 ± 0.15 at 1.0 mg/ml, 4.1 ± 0.31 at 2.0 mg/ml and 3.59 ± 0.42 at 4.0 mg/ml. The results were not significant. The effect of ERC extract on contraction frequencies in pregnant uterine strips in the presence of OXT and PGF 2α. is shown in Figure 41 (iv). Mean ± SEM uterine contraction frequencies during the negative control period was 2.72 ± 0.56. Following addition of extract in the presence of hormones, the mean ± SEM uterine contraction frequencies were 4.11 ± 0.38 at 0.5 mg/ml, 4.39 ± 0.4 at 1.0 mg/ml, 4.46 ± 0.38 at 2.0 mg/ml

and 4.06 ± 0.67 at 4.0 mg/ml. The results were significant ($P< 0.05$) only at 1.0 and 2.0 mg/ml.

3.2.3.6 Summary of the effect of ERC extract on uterine strips

Figure 43 shows in summary a comparison of the effects of ERC extract on contraction frequencies of non pregnant and pregnant uterine strip in the presence and absence of OXT and PGF 2α. The results were significantly different only at 1.0 and 2.0 mg/ml in pregnant uterine strips in the presence of OXT and PGF 2α only. The rest of the results were not significant.

3.2.3.7 Effect of chloroform *Ricinus communis* extract (CRC)

The non pregnant uterine strip responded to the chloroform (CRC) extract with a prolonged relaxation. There was no initial strong contraction as seen with aqueous and ethanol extracts of both plants. This response was seen both in the presence and absence of OXT and PGF 2α, Figure 44 (ii) and iii). Upon recovery the contractions were slower than control for all the uterine strips in pregnant and non pregnant in presence and absence of OXT and PGF 2α. In pregnant uterine strips in the presence of OXT and $PGF_{2\alpha}$, Figure 44 (iv), however there was a strong initial contraction (6.5 ± 0.01 amplitude) which was sustained briefly after which the contractions went back to normal.

FIGURE 41: The effect of ERC extract on uterine contraction pattern in pregnant and non pregnant uterine strips

(i) Contraction pattern of negative control (de jalon alone)

(ii) Contraction pattern of non pregnant uterine strips at low doses (0.5 and 1.0 mg/ml)

(iii) Contraction pattern of non pregnant uterine strips at medium dose (2.0 mg/ml) in t presence of OXT and PGF 2α.

(iv) Contraction pattern of pregnant uterine strips at high dose (4.0 mg/ml) in the prese of OXT and PGF 2α.

The ERC extract had no significant effect on the strength of contraction of either non preg or pregnant uterine strips.

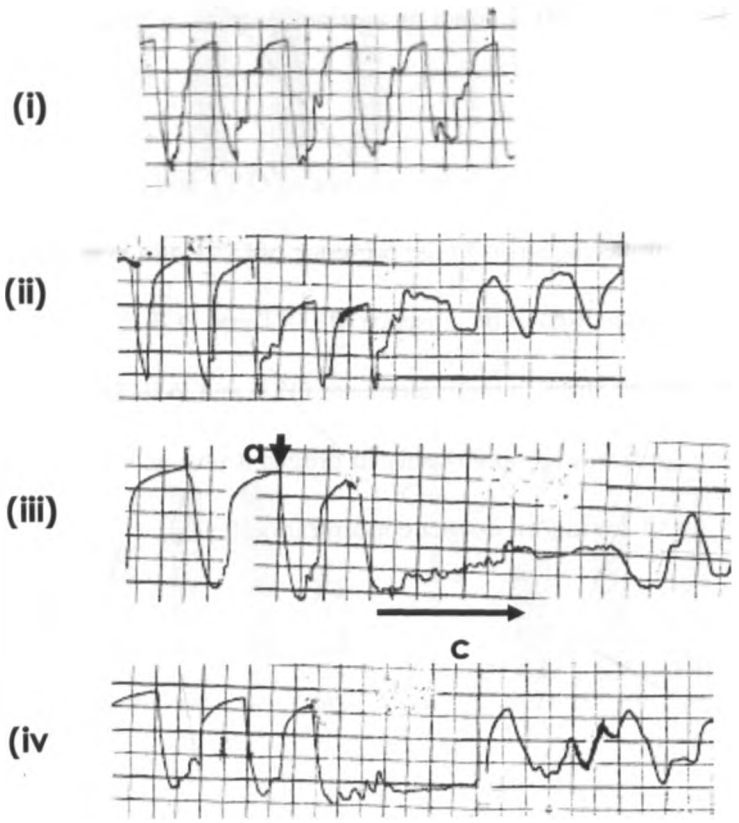



FIGURE 41: The effect of ERC extract on uterine contraction pattern in pregnant and non pregnant uterine strips

Key: **a**- point of extract infusion **c**- Sustained contraction phase.

FIGURE 42: The effect of ERC extract on uterine contraction frequency in pregnant

pregnant strips.

(i) Non pregnant uterine strips in the absence of OXT and PGF 2α.

(ii) Non pregnant uterine strips in the presence of OXT and PGF 2α

(iii) Pregnant uterine strips in the absence of OXT and PGF 2α.

(iv) Pregnant uterine strips in the presence of OXT and PGF 2α.

The results were significant ($P < 0.05$) only in pregnant uterine strips in the presenc

and PGF 2α at 1.0 and 2.0 mg/ml extract concentration levels.

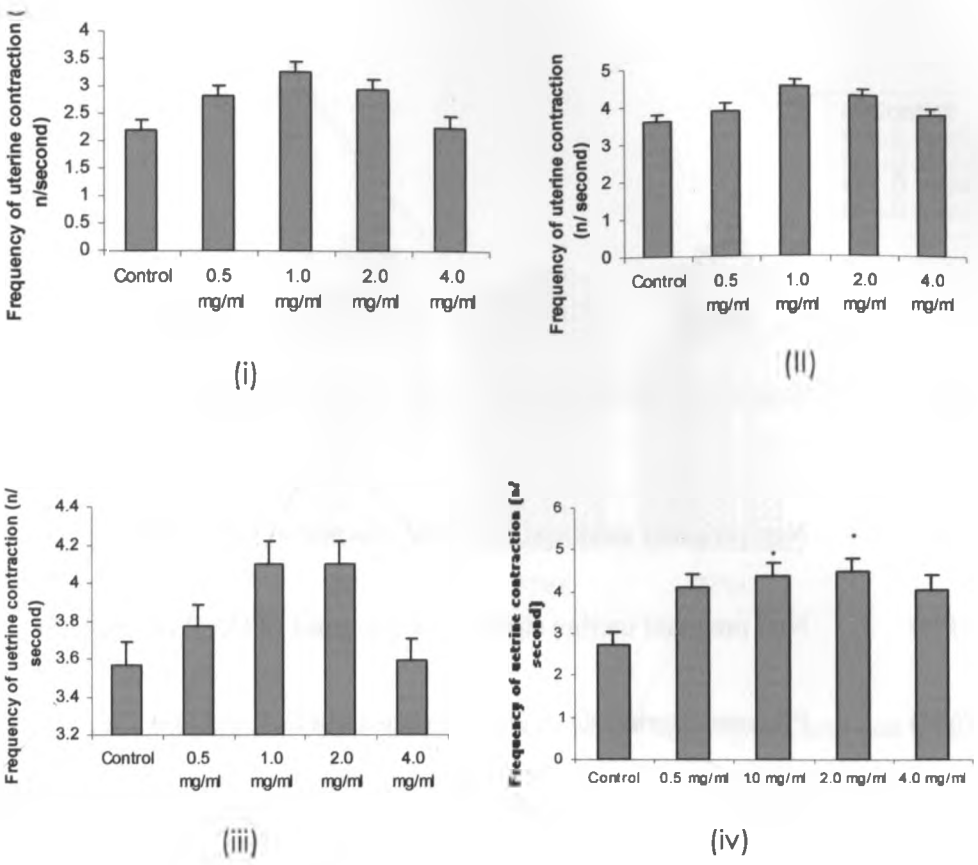



FIGURE 42: The effect of ERC extract on uterine contraction frequency in pregnant and non pregnant strips.

(v) Non pregnant uterine strips in the absence of OXT and PGF 2α.

(vi) Non pregnant uterine strips in the presence of OXT and PGF 2α

(vii) Pregnant uterine strips in the absence of OXT and PGF 2α.

(viii) Pregnant uterine strips in the presence of OXT and PGF 2α.

*P< 0.05

FIGURE 43: Comparisons of the effect of ERC extract on pregnant and non pregna strips

(NN) Non pregnant uterine strips in the absence of OXT and PGF 2α

(NPH) Non pregnant uterine strips in the presence of OXT and PGF 2α

(PNH) Pregnant uterine strips in the absence of OXT and PGF 2α

(PPH) Pregnant uterine strips in the presence of OXT and PGF 2α

The results were significant ($P < 0.05$) only in pregnant uterine strips in the presenc and PGF 2α at 1.0 and 2.0 mg/ml extract concentration levels.

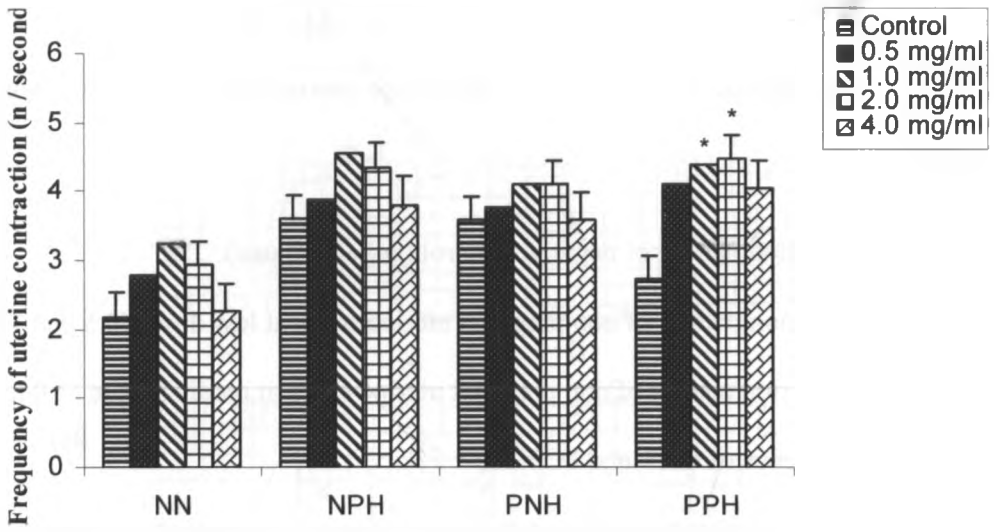



FIGURE 43: Comparisons of the effect of ERC extract on pregnant and non pregnant uterine strips

(NN) Non pregnant uterine strips in the absence of OXT and PGF 2α

(NPH) Non pregnant uterine strips in the presence of OXT and PGF 2α

(PNH) Pregnant uterine strips in the absence of OXT and PGF 2α

(PPH) Pregnant uterine strips in the presence of OXT and PGF 2α

(* $P<0.05$)

FIGURE 44: The effect of CRC extract on uterine contraction pattern in pregnant and non pregnant strips.

(i) Contraction pattern of negative control (de jalon alone)

(ii) Contraction pattern of non pregnant uterine strips at low doses (0.5 and 1.0 mg/ml)

(iii) Contraction pattern of non pregnant uterine strips at medium dose (2.0 mg/ml) in the presence of OXT and PGF 2α.

(iv) Contraction pattern of pregnant uterine strips at high dose (4.0 mg/ml) in the presence of OXT and PGF 2α.

The non pregnant uterine strip responded with a prolonged relaxation. This response was seen both in the presence and absence of OXT and PGF 2α, Figure 44 (ii and iii). In pregnant uterine strips in the presence of OXT and PGF 2α, Figure 44 (iv) there was a strong initial contraction which was sustained briefly after which the contractions went back to normal.

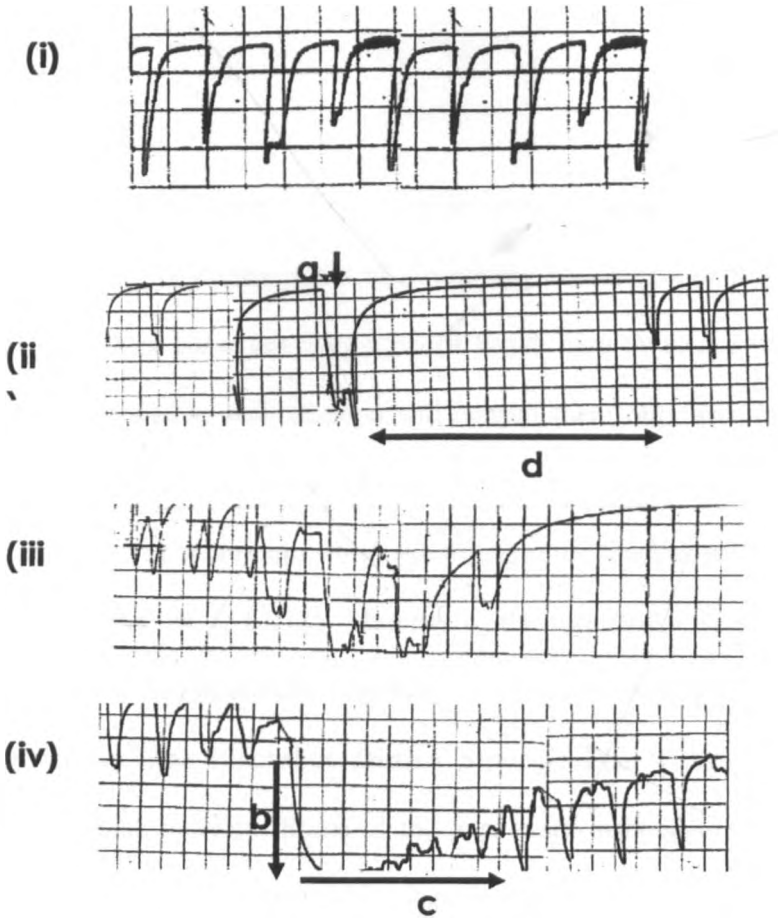



FIGURE 44: The effect of CRC extract on contraction pattern in pregnant and non pregnant uterine strips.

Key: **a**- point of extract infusion **b**- a strong initial contraction (Figure 44 iv only) **c**- sustained contractions (Figure 44 iv) **d**- prolonged relaxation without the initial strong contraction (Figure 44 ii and iii).

# CHAPTER FOUR

## 4.1 DISCUSSION

From time immemorial plants have been an indispensable source of both preventive and treatment of ailments in rural parts of developing countries. For 80% of rural poor, herbal medicine is in most cases the only form of health care (WHO, 1977). Even when trained physicians are available, sick persons will consult them only as a last resort (Kamatenesi-Mugisha and Origa, 2007). Some of the contributing factors to inadequate access to health care are, the doctor: patient ratio which according to the Machakos District Development Plan (2003- 2008) stands at 1: 62,325. Majority of the rural folks have to travel long distances (average 5 kilometers) in search of medical services as most health facilities are concentrated in urban centers. The Machakos District Strategic Plan (2005-2010) identified gaps in reproductive health delivery. Some of the gaps were inadequate skills by the reproductive health staff, unsafe motherhood and inadequate access to affordable quality service. Some of the documented conditions under reproductive health care in Kyevaluki and Kathiani Sub locations of Machakos and Kangundo Districts are delayed labor, protracted labor, post partum hemorrhage, retained after birth, vomiting during gestation, pregnancy edema and anemia, vaginal bleeding, threatened first, second and third trimester abortion / miscarriage and lack of milk expression during the immediate post partum period. According to the WHO report 2003, maternal related conditions is the number one cause of death and disease burden followed by malaria and HIV/ AIDS. The most important barrier to women health include distance to health facilities, health care costs, lack of funds and lack of reliable transport to and from the health facilities (Barton and Wamai,1994).

The ethno-botanical survey section of this study has demonstrated that the prevalence of herbal medicine use during pregnancy in the study area is similar to those reported by other studies not just in Africa and other developing countries, but even in parts of the developed world like China (Chuang et al., 2009), Norway (Nordeng and Havnen, 2004) and Taiwan (Chuang et al., 2007). The significance of the findings of this study for nursing / midwifery audience is worth highlighting since nurses can play an important role in the risk reduction of drug safety. In October 2004, WHO launched the World Alliance for Patient Safety in response to a World Health Assembly resolution 2002 urging WHO and member states to pay the closest possible attention to the problem of patient safety (WHO, 2004). Drug safety is an important part of patient safety thus the important role of nursing in pharmacovigilance is followed with interest (Ulfvarson et al., 2007; Chuang et al., 2009). For pregnant or post partum women, nurses or midwives are in a key position to evaluate adverse drug effects and educate them on dangers of possible expression of bioactive components of herbs in breast milk. Other studies have shown that herbs used during the first trimester caused a high risk of fetal congenital malformations (Chuang et al., 2006a).

The aim of the first part of this study was to investigate the prevalence of medicinal herbs as administered by TBA during pregnancy. The ethno-botanical cross sectional investigation carried out in Kathiani and Kyevaluki sub locations of Machakos and Kangundo districts in the present study identified 57 medicinal plants for the management of pre and post partum complications. 14 plants used for the management of delayed labor, post partum hemorrhage, prevention of first, second and third trimester abortion, pregnancy edema and anemia were however considered as morpho species (Okello and Ssegawa, 2007) since they lacked

identification characters and were difficult to find during the field excursions because of their rarity. As reported by Kamatenesi- Mugisha et al., (2007) the main methods for herbal preparation are boiling, squeezing and pounding and the most common route of administration was oral. In the study a few of the plants were crushed and smeared over the abdomen as was demonstrated in this study as well. The widespread use of herbs during the pre partum period reported in this study is similar to studies carried out in China and Taiwan (Chen and Wang, 2000; Chuang et al., 2007).

The present study revealed that the majority of practicing TBA were females. These women are respected members of the community not just because of their practice but also due to their age, most of them were between the ages 40-50 years (elderly citizens). Almost half of them had practiced for more than five years, 64% of them having attended to more than two hundred pregnant women during the course of their practice. Despite their low level of education all the TBA exhibited sound hygienic practices during herbal preparation. This is in agreement with what has been reported previously by (Okello and Ssegawa, 2007). Due to their proximity and accessibility within the community, pregnant mothers tend to trust and consult the TBA all the time. The TBA on their part, according to this study managed pregnancy complications during the entire gestation period. They monitored labor, supervised the actual parturition and visited both mother and infant during the immediate post partum period. This additional psychosocial support provided by TBA during labor and the immediate post partum period is not available in health centers. It is this close relationship between the TBA and her/his patients that is cherished by many rural women and explains the continued existence of TBAs. Long distances to hospital and unreliable public transport

system probably contributed towards 55% of the mothers opting to deliver at home despite the risks involved. A good number of the TBAs clients (35%) also cited lack of finances as their reason for consulting the TBA as they could not afford to deliver in hospital, thus corroborating the findings of Barton and Wamai (1994) regarding the constraints that drive pregnant women in the rural areas to consult TBAs. Chuang et al. (2009) on the other hand, reported that high levels of education in women aged 24 to 30 years; primipara and presence of chronic illnesses were some of the factors that led to herbal medicine consumption by pregnant women. This is in contrast to the results shown in this study, where low levels of education, presence of readily available and affordable TBAs services in the community, threatened abortion, provision of psychosocial support by TBAs during labor, and long distances to hospitals, were all contributing factors to herbal medicine consumption by pregnant women. An interesting finding in this study was also the fact that 30% of the clients reported having previously been abused by RHW and were therefore not willing to deliver in Hospital. Several clients additionally consulted TBAs during the course of gestation due to vaginal bleeding, delayed labor, dizziness and lower abdominal pain. Most plants claimed by TBAs to be uterine stimulants are used to induce and maintain labour, help remove the retained placenta, regulate post partum bleeding and as abortifacient (Kamatenesi-Mugisha and Origa, 2007). The plants are taken towards the end of gestation period or at the onset of labour pains.

All pregnancies that had exceeded 40 weeks were considered as cases of delayed labor. TBAs used several remedies to initiate labor. Quite a few of the TBAs (31%) however, immediately referred such patients to hospital. It is worth noting that most of those who referred patients to hospital had some level of education (completed primary and/or secondary education). This

perhaps enabled them appreciate the risks involved in administering herbs to pregnant mothers especially with a complication like delayed labor. Interestingly enough, a small number of TBAs relied on divine intervention (prayers to ancestors) to help them handle the patients with delayed labor. All plants were harvested from the wilderness and their knowledge and presence therefore kept within a small cycle of traditional practitioners which however, brings into focus the need to conserve these precious plants. The types of plants used in the management of delayed labor were few, which would probably indicate that the condition is relatively rare within the community as reported also by Kamatenesi -Mugisha and Origa (2007).

Several TBAs explained protracted labor as being due either to witchcraft or the pregnant woman having offended her mother-in-law. However, as was the case with delayed labor, relatively few plants were reportedly used for this condition, indicating again the rare occurrence of it in the community. Post partum hemorrhage (PPh) is on the other hand the single leading cause of maternal mortality and morbidity in developing countries and a concern even in developed countries (WHO, 2003). More than half of all maternal deaths occur within 24 hours of delivery, mostly from excessive bleeding. Active management of the third stage of labor has been proven to reduce the incidence of PPh and involves interventions designed to facilitate the delivery of the placenta (afterbirth) by increasing uterine contractions and preventing PPh by averting uterine atony. In health centers PPh management is through administration of uterotonic agents, controlled umbilical cord traction and abdominal massage. In this study some of the TBAs reported abdominal massage as one of their methods for management of PPh. Unfortunately TBAs rarely use gloves while helping mothers during parturition. This is a dangerous practice as it is a contributing factor in HIV /

AIDS transmission from mother to TBAs and vice versa. The TBAs could handle more than one pregnant woman routinely and could therefore transmit the virus from client to client. It is therefore important for national health professionals to advocate for skilled care at birth; educate the public on the need for adequate prevention and treatment of post-partum hemorrhage; incorporate active management of the third stage of labor into the curricula for all skilled birth attendants and collaborate with national pharmaceutical regulatory agencies, policy makers and donors to ensure a consistent supply of uterotonics in hospitals. It is also imperative to train TBAs on dangers involved in the transmission of HIV / AIDS and other STDs during parturition and the importance of referrals in order to reduce maternal mortality. The results of this study indicate that several pregnant women with signs of threatened abortion readily use herbal remedies. This is similar to what was reported in a study carried out by Chuang et al. 2005 and 2007. In this study, several plants were identified for the prevention of abortion during the course of the pregnancy. The large number of plants indicates that the condition is relatively common within the community and could be a situation for the health sector to look into. Considering that prevalence of infertility could be linked to previous abortion(s), patients who have undergone abortion or miscarriage in the hands of TBAs and/or through use of herbs could have their future reproductive function compromised by secondary infertility.

First trimester vomiting is one of the commonest pregnancy related conditions and its persistence could lead to further complications like anemia as most mothers feed poorly during this period. The large number of medicinal plants used for the management of this condition as well as pregnancy edema does confirm that these complications are common within the community. It is important to note that most TBAs (69%) acquire their knowledge

from family members and only a small number (18%) tend to learn from practicing TBAs. This indicates a cultural practice being passed down from parents to children. *In vitro* studies on the two plants *Euclea divinorum and Ricinus communis* yielded some interesting results. *Euclea divinorum* plant is used for firewood and as walking sticks (Kokwaro, 1993). The bark is added to soup as an appetizer and the branches used as tooth brushes (Kokwaro, 1993). The root, bark and leaves have been used for medicinal purposes (Kokwaro, 1993) but to the best of my knowledge there has been no literature on its potency as a uterotonic agent. The success of pregnancy depends on the ability of the myometrium to maintain quiescence throughout the duration of the gestation period. Premature onset of uterine contraction is often the cause of abortion or miscarriage. On the other hand inadequate and infrequent contractions can result in delayed, obstructed, protracted labor and retained after birth. The herbs are administered in the latter part of gestation, during labor and the immediate post partum period, to ease the parturition process and manage cases of post partum hemorrhage and retained after birth. The result of this study indicates that AED extract not only mimicked oxytocin more closely than the other extracts but also had the greatest effect on the initial contraction strength as well as greater increase of resumed contraction frequencies following exposure. This would suggest that the active compound is not only water soluble but also perhaps more stable in aqueous form than in polar solvents. Considering that the extracts used by TBAs are prepared in water, these findings strongly suggest the presence / existence of an oxytocin like compound in the plants especially *Euclea divinorum*. It is tempting to argue that when consumed by pregnant women, the aqueous and to a smaller extent ethanol extracts of both plants would augment endogenous oxytocin / prostaglandin effects and cause parturition. The extract had a dose dependent augmenting effect both on the amplitude and frequency of uterine strip contraction.

The effect was greater in pregnant compared to non pregnant uterus and was enhanced further when pregnant uteri were exposed to the extract in the presence of OXT and PGF2α. These results support the traditional use of *Euclea divinorum* concoctions in the initiation of labor, management of protracted labor, post partum hemorrhage and retained after birth. Physiologically, during labor and the immediate post partum period, levels of oxytocin and prostaglandins are high within the uterus. The crude plant extracts were able to exert maximum augmenting effect during this time and hence the enhanced effect on pregnant rabbit uterus. Ethanol *Euclea divinorum* (EED) extract had a similar effect on uterine contraction frequency and strength when compared to aqueous *Euclea divinorum* (AED) extract. The greatest effect in this case is also on the initial contraction. The EED extract however seemed to have a longer residual effect compared to AED as during the recovery phase, the resumed contractions were more frequent but of smaller magnitude. Both aqueous and ethanol extracts of *Euclea divinorum* seem to have the same mechanism of action since both had an enhanced effect on strength and frequency of uterine contraction especially in the pregnant uterine strip.

Aqueous *Ricinus communis* extract also had an enhanced effect both on amplitude and frequency of uterine muscle contraction in a dose dependent manner. Upon recovery the uterus contraction frequency increased but the contraction never resumed the negative control pattern. The highest contraction frequencies were noted in pregnant uteri in the presence of OXT and PGF2α. Ethanol *Ricinus communis* extract however had no significant effect on the amplitude and frequency of uterine contraction in non pregnant uterine strip. Even in the pregnant uterine strip, the contraction frequency was only significant at 1.0 and 2.0 mg/ml extract dose levels in the presence of OXT and PGF 2α. The results seem to indicate that

ethanol *Ricinus communis* extract's mechanism of action maybe different from that of aqueous *Ricinus communis* as well as aqueous and ethanol *Euclea divinorum*. This is however only an indication and many more studies are required before any conclusions can be made. The uterine response to chloroform *Euclea divinorum* (CED) *and Ricinus communis* (CRC) was the same in non pregnant uterine strips. The chloroform extracts caused a prolonged relaxation of the uterine strip even in the presence of OXT and PGF 2α. The CRC extract response was however different in the pregnant uterine strip in the presence of OXT and PGF 2α. In this case the uterine strip had an initial sharp contraction similar to AED, EED and ARC instead of a relaxation. The resumed contractions following CRC were also more frequent than in the non pregnant uterine strips exposed to both CED and CRC extract. Probably in the pregnant uterine strip, the presence of additional OXT and PGF 2α masked the effects of active relaxants in chloroform extracts. Oxytocin is one of the most potent uterotonic agents known, and its effect on uterine contractility is of major pharmacological importance. Medicinal plants that can be used to induce labor, treat post partum hemorrhage and retained after birth are of great importance especially in rural parts of developing countries where hospitals are far from rural homesteads and have inadequate supplies of emergency medicine.

The oxytocin receptor belongs to the G-protein coupled receptor family. After binding oxytocin, the receptor activates phospholipase- Cβ by coupling to GTP binding proteins (Ku et al., 1995). This leads to the generation of the two second messengers: inositol 1,4,5-triphosphate (IP3) and diacylglycerol (DAG). Both second messengers are believed to be involved in the generation of the physiological myometrium response to oxytocin (Shlykov

and Sanborn, 2004). Oxytocin thus acts through its G-protein coupled membrane receptors whose activation in the myometrium results in a cascade of events that trigger the activation of myosin light chain-kinase activity which initiates myometrium contractions (Sanborn et al. 1998; Bafor et al. 2010). Oxytocin also induces $PGE_2$ synthesis in uterine endometrial cells. This increase in local prostaglandin production further stimulates uterine contraction. A possible involvement of voltage operated calcium channels in *Ficus exasperata* induced uterine contractions has been suggested (Bafor et al., 2010). According to Bafor et al. 2010 however, *Ficus exasperata* may also have a direct receptor effect which is linked via second messenger of calcium and hence calcium channels. *Ficus exasperata* according to Bafor et al. (2010) may also stimulate uterine contractions via activation of α adreno-ceptors present in the uterus. Similar oxytocic effects were seen in this study where AED extract enhanced both amplitude and frequency of contraction, ARC extract enhanced frequency of resumed contractions and EED extract enhanced the amplitude of contraction. The multiple components in the effect of oxytocin could be due to its action on different cell types within the myometrium. At least three distinct components can be discerned in the effect of oxytocin on human uterine smooth muscle; (1) increase in frequency of contractions; (2) initial transient increase in the base tone (incomplete relaxation); (3) long lasting increase in the amplitude and duration of phasic contractions (Shmygol et al., 2006). Shmygol et al. (2006) further identified interstitial cells of Cajal (ICC) in the myometrium which might mediate changes in contraction frequencies whereas smooth muscle cells are responsible for the increase in amplitude of contraction. It is thus possible that the extracts in this study affected both interstitial cells of Cajal and smooth muscle cells that control contraction strength.

Cytoplasmic $Ca^{2+}$ concentration also determines myometrial contraction (Wray et al., 2003). As is already mentioned in the literature, whole uterine tissue comprises an outer myometrium and inner endometrium (Veale et al., 2000). Oxytocin acts on the myometrium oxytocin receptors subtype 1a ($OT_{1a}$) to directly cause uterine contraction and on endometrial oxytocin receptors type 1b ($OT_{1b}$) to stimulate prostaglandin synthesis and release (Chan et al., 1983), hence it has dual action in the uterus. This pharmacological differentiation has been shown in both the rat uterus and pregnant human uterus (Veale et al., 2000). Prostaglandins are however synthesized also in response to other hormonal stimuli like oxytocin. The uterine myometrium as already mentioned also comprises longitudinal and circular smooth muscles. The response to oxytocin has been found to be more potent in the longitudinal layer than in the circular layer (Tuross et al., 1987). The myometrium, for example rat myometrium, contracts in response to prostaglandin F (PGF) and prostaglandin E (PGE) stimulation (Kariyama and Suzuki, 1976). $PGF_{2\alpha}$ and $PGE_2$ promote uterine smooth muscle contraction by interaction with $EP_1$, $EP_3$ and FP receptors in plasma membrane of humans, rats and other species (Veale et al., 2000).

Several authors have attempted to unravel the effects of herbal extracts on this complex uterine tissue. Aqueous extract of *Agapanthus africanus* for instance was found to stimulate smooth muscle directly and to augment the initial response of the uterus to oxytocin and acetylcholine (Kaido et al., 1997; Veale et al., 1999). The results of this study indicate that the rabbit myometrium response to the extracts was stronger in the presence of oxytocin and prostaglandin $F_{2\alpha}$ suggesting also an augmenting effect of both aqueous and ethanol extracts of *Euclea divinorum* and *Ricinus communis*. Aqueous *Euclea divinorum* extract enhanced

uterine contractility more strongly than ethanol *Euclea divinorum* suggesting it was the most potent of the extracts, especially since ethanol *Euclea divinorum* was still more potent than

both aqueous *Ricinus communis* and ethanol *Ricinus communis.* In this study, oxytocin was used or studied in the presence of prostaglandin to simulate the normal mammalian female situation. The uterus of the rat and perhaps other mammals also possess myometrial muscarinic receptors and therefore will respond by contraction upon stimulation of cholinergic nerves or by agonistic agents like acetylcholine. Aqueous extract of *Agapanthu africanus* leaves were found to exhibit agonist activity on uterine muscarinic receptors and promoted the synthesis of prostaglandins in the oestrogenized rat uterus.

It is thus obvious that the interaction of herbal components with uterine contractile elements could be multifaceted and complex and hence require many more detailed studies. Although this study has not proceeded to the level of isolating biological active components, it is very possible that the herbs in this study *Ricinus communis* and *Euclea divinorum* could also contain tannins said to be commonly present in most herbal extracts (Bafor et al., 2009) especially since tannins are found in ethanolic , methanolic and aqueous extracts. The tannins as reported by Calixto et al. (1986); Raju et al, (2004) and Bafor et al. (2009) could then contribute to the contractility of the uterine myometrium exhibited in this study.

The isolated oestrogenized rat uterus preparation is a model well suited to pharmacological investigations of contractile activity in the uterine smooth muscle and is used extensively by reproductive pharmacologists. In this study oestrogenized rabbit uterine preparations were used and have so far shown that this model can also give indications as to the effect of herbal extracts. Basic initial pharmacological screening procedures, which identify direct uterine

smooth muscle activity in crude plant extracts need to be followed by more detailed studies which characterize the pharmacological activity of the phytomedicine as fully as possible. This study has provided such basic initial pharmacological screening that has identified uterine smooth muscle activity in crude plant extracts of *Euclea divinorum* and *Ricinus communis.* The data from this study can thus provide a basis for further investigations and act as guideline in planning more definitive pharmacological and biochemical tests.

## 4.2 CONCLUSION AND RECOMMENDATION

The study has documented the medicinal plants used by TBAs for the management of pregnancy and post pregnancy complications. For most of the plants, the part used most is the root, meaning the rest of the plant is wasted. It is recommended that other plant parts (stem and leaves) should be tested for pharmacological activity. If positive then the TBAs should be educated to use the rest of the plant parts in order to minimize natural resource depletion. A more thorough documentation of medicinal plants used by TBAs should also be undertaken to not only preserve the knowledge for future generation but also generate affordable and effective ethno medicine for the management of reproductive ailments in rural set up. Medicinal plants used in the management of disorders and ailments that cause gynecological morbidity are capable of producing good results in the health and well being of women (Pampolana- Roger, 2000). This study for instance has shown evidence of the presence of oxcytocic compound in the extracts which provides a scientific basis for their use by TBAs. All that is required is proper studies and documentation.

The study has also successfully demonstrated the effect of extracts of two of the plants on the rabbit myometrium. The result of this study indicates that AED extract augmented oxytocin

induced uterine contractions more than the other extracts and had the greatest effect on the initial contraction strength as well as greater increase of resumed contraction frequencies following exposure. For both plants the most effective dose appeared to be 2.0 mg/ml. in the organ bath. However more research is definitely needed in this area. In this study for instance, oxytocin and prostaglandin were not studied separately and hence their individual interaction with the extracts could not be ascertained.

As a way forward therefore, many more studies should be undertaken in the future not only to document the effect of the two hormones but also to isolate, identify and characterize the active components including oxytocic components in *Euclea divinorum* and *Ricinus communis* plants and to elucidate the component's mechanism(s) of action.

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TRADITIONAL BIRTH ATTENDANT QUESTIONAIRRE

Dear respondent

I am a student at the University of Nairobi pursuing a Master of Science degree in Reproductive Biology. Kindly support me in completing my research work for the project through answering the questionnaire presented to you. The purpose of the questionnaire is to get information for my project: whose title is **"An in vitro study of *Ricinus communis* and *Euclea divinorum* extracts on isolated rabbit uterus"**.

The information gathered from this research will be treated in utmost confidentiality, as it will only be used for academic purposes.

Best regards

Catherine Kaluwa Kaingu Reg no. J56/ 7119/ 2006.

Signature:……..

REPRODUCTIVE HEALTH MANAGEMENT- TRADITIONAL PERSPECTIVE

Division: Population

Location: Population

Sub location: Population

Name

Age A) 40-50 [ ] b) 51-60[ ] c) 61-70 [ ] d) Over 70 [ ]

Sex Female [ ] Male [ ]

Marital status Single [ ] Married [ ] Widowed [ ]

Education level: None [ ] Primary [ ] Secondary [ ]

College [ ]

TBA number of children 1-3 [ ] 4-6 [ ] 7-9 [ ]

How were you initiated into current occupation? Trained [ ] Inherited [ ]

Divine intervention [ ]

For how long have you been in practice? Less than 5 years [ ] 1-5 years [ ]

More than 5 years [ ] More than 10 years [ ]

What is the total number of women you have attended to date?

More than 50 [ ] More than 100 [ ] More than 200 [ ]

How do you handle **delayed labor**?

Divine intervention [ ]

Herbal remedy [ ]

Refer to hospital [ ]

Divine plus herbs [ ]

Massage [ ]

What part of the plant is used?

Root [ ]

Stem [ ]

Leaves [ ]

Root bark [ ]

Stem bark [ ]

Massage and herbs [ ] Massage and divine intervention [ ]

Specify the herbs if any.....

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind and filter. Give patient to chew [ ]

Clean part of the plant, grind, add water, [ ]

What is the dose level and how often is it given?

300ml once a day [ ] Other.....specify

300 ml three times daily [ ]

Half glass three times daily [ ] 300ml three times daily for 7 days [ ]

150ml three times daily for 7 days [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb used Yes [ ] No [ ]

In case you are unable to handle, what is your immediate line of action

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you manage cases of **protracted labor?**

What part of the plant is used?

| | | | |
|---|---|---|---|
| Divine intervention | [ ] | Root | [ ] |
| Herbal remedy | [ ] | Stem | [ ] |
| Refer to hospital | [ ] | Leaves | [ ] |
| Divine plus herbs | [ ] | Root bark | [ ] |
| Massage | [ ] | Stem bark | [ ] |
| Massage and herbs | [ ] | Massage and divine intervention | [ ] |

Specify the herbs if any.....

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind and filter. Give patient to drink [ ]

Clean part of the plant, grind, add water [ ]

What is the dose level and how often is it given?

300ml once a day [ ] Other.....specify

300 ml three times daily [ ] Half glass three times daily [ ]

One glass, 3 times daily for 1 week [ ] Half glass three times daily for 1 week [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb used Yes [ ] No [ ]

In case you are unable to handle, what is your immediate line of action

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you handle **obstructed labor**?

Divine intervention [ ]

Herbal remedy [ ]

Refer to hospital [ ]

Divine intervention plus herbs [ ]

Massage [ ]

Massage and herbs [ ]

What part of the plant is used?

Root [ ]

Stem [ ]

Leaves [ ]

Root bark [ ]

Stem bark [ ]

Massage and divine intervention [ ]

Specify the herbs if any.....

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind and filter. Give patient to drink [ ]

Clean part of the plant, grind add water [ ]

What is the dose level and how often is it given?

1 glass per day[ ] Specify other.....

1 glass three times daily [ ] Half glass three times daily [ ]

One glass, 3 times daily for 1 week [ ] Half glass three times daily for 1 week [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb? Yes [ ] No [ ]

In case you are unable to handle the case, what is your immediate line of action?

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you handle **Post parturition hemorrhage**? Specify herbs……...

Divine intervention [ ] Herbal remedy [ ] Refer to hospital [ ]

Divine plus herbs [ ] Massage [ ] Massage and herbs [ ]

Massage and divine intervention [ ] Has never handled such patients [ ]

What part of the plant do you use?

Root [ ] Stem bark [ ] Stem [ ] Leaves [ ] Root bark [ ]

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind and filter, then give patient to chew [ ]

Clean part of the plant, grind add water [ ]

What is the dose level and how often is it given?

1 glass per day[ ] Other……specify

1 glass three times daily [ ] Half glass three times daily [ ]

One glass three times daily for 1 week [ ] Half glass three times daily for 1 week [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb used Yes [ ] No [ ]

In case you are unable to handle, what is your immediate line of action?

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you handle **retained after birth**?

Divine intervention [ ] Specify the herbs if any ....

Herbal remedy [ ] Refer to hospital [ ]

Divine plus herbs [ ] Massage [ ]

Massage and herbs [ ] Massage and divine intervention [ ]

Does not handle [ ] Manual removal [ ]

What part of the plant do you use?

Root [ ] Stem bark [ ] Stem [ ] Leaves [ ] Root bark [ ]

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind and filter. Give patient to chew [ ]

Clean part of the plant, grind add water [ ]

What is the dose level and how often is it given?

1 glass per day[ ] Other.....specify

1 glass three times daily [ ] Half glass three times daily [ ]

One glass 3 times daily for 1 week [ ] Half glass three times daily for 1 week [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb? Yes [ ] No [ ]

In case you are unable to handle, what is your immediate line of action?

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you handle **lack of milk let down** after parturition?

Divine intervention [ ] Advice of nutrition [ ] Herbal remedy [ ]

Does not handle [ ] Refer to hospital [ ] Divine plus herbs [ ]

Massage [ ]Massage and herbs [ ] Massage and divine intervention [ ]

Specify the herbs if any.....

What part of the plant do you use?

Root [ ] Stem bark [ ] Stem [ ] Leaves [ ]

Root bark [ ]

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind and filter. Give patient to chew [ ]

Clean part of the plant, grind add water [ ]

What is the dose level and how often is it given?

1 glass per day[ ] Other.....specify

1 glass three times daily [ ] Half glass three times daily [ ]

One glass, 3 times for 1 week [ ] Half glass three times daily for 1 week [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb used? Yes [ ] No [ ]

In case you are unable to handle the case, what is your immediate line of action?

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you handle **early pregnancy bleeding disorder**?

Divine intervention [ ] Herbal remedy[ ] Does not handle [ ]

Refer to hospital [ ] Divine intervention and herbs [ ] Massage [ ]

Massage and herbs [ ]

Specify the herbs if any.....

What part of the plant do you use?

Root [ ] Stem bark [ ] Stem [ ] Leaves [ ]

Root bark [ ]

How do you prepare the herbs?

Clean root, grind, filter and add warm water [ ]

Clean root, peel, grind and filter. Then give patient to chew [ ]

Clean part of the plant, grind add water [ ]

What is the dose level and how often is it given?

1 glass per day[ ] Other.....specify

1 glass three times daily [ ] Half glass three times daily [ ]

One glass, 3 times daily for 1 week [ ] Half glass three times daily for 1 week [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb? Yes [ ] No [ ]

In case you are unable to handle, what is your immediate line of action?

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you handle **threatened abortion in 2nd and 3rd trimester?**

Divine intervention [ ] Herbal remedy [ ] Does not handle [ ]

Refer to hospital [ ] Massage [ ] Massage and herbs [ ]

Massage and divine intervention [ ]

Specify the herbs if any.....

What part of the plant do you use?

Root [ ] Stem bark [ ] Stem [ ] Leaves [ ] Root bark [ ]

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind and filter. Give patient to chew [ ]

Clean part of the plant, grind add water [ ]

What is the dose level and how often is it given?

1 glass per day [ ] Specify other.....

1 glass three times daily [ ] Half glass three times daily [ ]

One glass, 3 times daily for 1 week [ ] Half glass three times daily for 1 week [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb? Yes [ ] No [ ]

In case you are unable to handle, what is your immediate line of action?

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you handle **edema** in pregnancy?

Massage affected area [ ] Advice on nutrition [ ] Herbal remedy [ ]

Does not handle [ ] Refer to hospital [ ]

Massage and herbs [ ] Massage and divine intervention [ ]

Specify the herbs if any.....

What part of the plant do you use?

Root [ ] Stem bark [ ] Stem [ ] Leaves [ ]

Root bark [ ]

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind and filter. Give patient to chew [ ]

Clean part of the plant, grind and add water [ ]

What is the dose level and how often is it given?

1 glass per day [ ] Specify other.....

1 glass three times daily [ ]

Half glass three times daily [ ]

One glass, 3 times daily for 1 week [ ] Half glass three times daily for 1 week [ ]

Is the herb easily available? Yes [ ] No [ ]

Is there an alternative herb? Yes [ ] No [ ]

In case you are unable to handle, what is your immediate line of action?

Refer to hospital [ ] Divine intervention [ ] Never been defeated [ ]

How do you handle **anemia** in pregnancy?

Advice on nutrition [ ] Herbal remedy [ ] Does not handle [ ]

Refer to hospital [ ]

Divine intervention and herbs [ ] Massage [ ]

Massage and herbs [ ]

Specify the herbs if any.....

What part of the plant do you use?

Root [ ] Stem bark [ ] Stem [ ] Leaves [ ]

Root bark [ ]

How do you prepare the herbs?

Clean roots, grind, filter and add warm water [ ]

Clean root, peel, grind add water and filter. Give patient to chew [ ]

TBA CLIENT QUESTIONAIRRE

Dear respondent

I am a student at the University of Nairobi pursuing a Master of Science degree in Reproductive Biology. Kindly support me in completing my research work for the project through answering the questionnaire presented to you. The purpose of the questionnaire is to get information for my project: whose title is **"An invitro study of *Ricinus communis* and *Euclea divinorum* extracts (plants commonly used by Traditional birth Attendants) on isolated rabbit uterus "**.

The information gathered from this research will be treated in utmost confidentiality, as it will only be used for academic purpose.

Catherine Kaluwa Kaingu J56 / 7119/ 2006

Signature……..

**REPRODUCTIVE HEALTH MANAGEMENT- TRADITIONAL PERSPECTIVE**

Division: Population

Location: Population

Sub location: Population

Name ……

Age group

16-20 [ ] 21-25 [ ] 26-30 [ ]

31-35 [ ] 36-40 [ ]

Sex Male [ ] Female [ ]

Marital status Widow [ ] Single [ ] Married [ ]

Education Primary [ ] Secondary [ ] College [ ]

None [ ]

No of children: 1-3 [ ] 4-6 [ ] 7-9 [ ]

Does the client breastfeed? Yes [ ] No [ ]

How soon does the baby start antenatal clinic?

Immediately after birth [ ] 2 weeks after [ ] One month after [ ]

Where did client deliver the baby? Home [ ] Hospital [ ]

If at home, why did you not go to health facility?

Readily available TBA [ ] Costly hospital [ ] Abusive RHW staff [ ]

Specify other.....

Who helped the client during labor?

Neighbor / relative [ ] TBA [ ] Self [ ]

Why did the client consult TBA during gestation and afterwards?

Friendly services [ ] Affordable service [ ] Readily available services [ ]

Highly recommended [ ]

Specify other reasons.....

How many times has client had babies? First time [ ] More than once [ ]

Have you ever attended any antenatal clinic? Yes [ ] No [ ]

At what stage of pregnancy did client consult TBA?

1st trimester [ ] 2nd trimester [ ] 3rd trimester [ ]

Specify other.....

What are the symptoms that made client consult TBA?

Bleeding [ ] Dizziness [ ] Delayed labor [ ]

Lower abdominal pain [ ] Discharge [ ]

Specify other reasons.....

What type of treatment / management was prescribed by TBA?

Massage [ ]Herbal remedy [ ] Refer to hospital [ ]

For topical application, what was the duration of treatment?

1 week [ ] 2 weeks [ ] One month [ ]

For oral use: what was the duration of treatment?

1 week [ ] 2 weeks [ ] One month [ ]

Was the treatment effective Yes [ ] No [ ]

If yes, After single treatment [ ] After several visits [ ]

How do you pay the TBA?

Material payment [ ] Monetary [ ]

If monetary how much per visit? Free [ ] Small fee [ ]

What is the distance from your home to the closest health facility?

0-2 Km [ ] 3-5 Km [ ] 6-9 Km [ ] More than 9 Km [ ]

What form of transport do you use when going to health facility?

By foot [ ] Bicycle [ ] Vehicle [ ]

Is form of transport readily available at all times? Yes [ ] No [ ]

TBAs SELECTION CRITERIA

The inclusion criteria for all TBAs was:

1. Willingness to participate in the interviews, focused group discussion and filling out of the TBA questionnaire without coercion.

2. All TBAs must be living in the study area.

3. The TBAs must be practicing at the time of the interviews.