TANG [HUMANITAS MEDICINE]

Original article

EVALUATION OF OXYTOCIN LIKE EFFECTS OF *Uvariodendron kirkii* (Verdec.) EXTRACTS ON ISOLATED UTERINE STRIPS OF WISTAR RATS

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ABSTRACT

Uterotonics have the ability to contract uterus. Such plants might be useful in augmenting or inducing labour, expelling retained afterbirth and for abortifacient purposes. Limitations associated with conventional treatments have made herbal medicines a feasible alternative for the management of these conditions. The aim of this study was to evaluate the contractile effects of *Uvariodendron kirkii* extracts on isolated uterine strips of female Wistar rats. Isolated strips of Wistar rats' uteri were treated with 20, 40, 80 and 160 mg/ml concentrations of *Uvariodendron kirkii* aqueous extract. The plant extract was also tested against prostaglandin and oxytocin induced uterine contractions. *Uvariodendron kirkii* extract concentrations (20, 40, 80 and 160 mg/ml) increased the frequency of uterine contraction (16.53, 25.12, 33.48 and 56.39 percentages respectively) compared to the control. The graded extract concentrations caused a significant increase in amplitude (force) of uterine contractions by 2.87, 9.22, 16.37 and 24.32 percentages respectively. The concentrations significantly increased the frequency of oxytocin induced uterine contractions by 6.92; 28.31; 47.06, 58.78 percentages respectively. The graded extract concentrations also significantly increased the amplitude of oxytocin induced uterine contractions by 6.07; 9.40; 15.19 and 23.56 percentages respectively. *Uvariodendron kirkii* extract concentrations significantly increased the frequency and amplitude of prostaglandin induced contractions. The percentage increase in frequency was 11.44, 8.92, 20.65 and 35.71 at 20, 40, 80 and 160 mg/ml respectively. The mean amplitude of prostaglandin induced uterine contractions also increased (4.75, 3.89, 8.29 and 15.91% at 20. 40, 80 and 160 mg/ml respectively). The extract caused a dose dependent increase in uterine frequency and amplitude of contraction. The findings of this study are useful in generating a novel uterotonic agent that will be useful in augmenting labour or in expelling retained after birth in cattle. More studies at molecular level will further elucidate the plant mechanism of action.

Keywords: *Uvariodendron kirkii*, Oxytocin induced, Prostaglandin induced, Uterine contractions

INTRODUCTION

Post-partum haemorrhage is the single leading cause of maternal morbidity and mortality in developing countries (Fukami *et al*., 2019). Maternal mortality occurs within 24 hours of childbirth, mostly from excessive bleeding (Ngwenya and Bulawayo, 2016). Medicinal plants that can be used to induce labour, treat post-partum haemorrhage and retained afterbirth are of great importance especially in rural parts of developing countries where health facilities are far and have inadequate supplies of emergency medicines (Kaingu *et al*., 2012). *Uvariodendron kirkii* (CK008) is a native plant in Tana River county, Kenya that is traditionally used to treat menorrhagia, dysmenorrhea, retained placenta and post-partum haemorrhage (Kaingu *et al.,* 2013). It has a fertility regulating effects such as anti-fertility and anti-implantation properties (Kaingu, 2016). The plant causes uterine contractions thereby explaining the anti-implantation effect. This study therefore, evaluated the contractile effects of aqueous root bark extracts of *Uvariodendron kirkii* on isolated rat uterine tissue in the presence and absence of oxytocin and prostaglandin F2α.

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MATERIALS AND METHODS

Collection and preparation of the plant material

The plant was harvested from Tana River County, Kenya. The plant material was collected specifically in the Itsowe, Garsen and Ngao subdivisions because of widespread use of herbal medicine and inaccessibility to health facilities (Kaingu *et al.,* 2013). *Uvariodendron kirkii* roots (CK008) were collected, dried, ground and the powder stored as per the method described in Kaingu *et al.,* 2017.

Extract preparation

As per method described by (Kaingu *et al.,* 2017). Extract was then weighed to determine yield.

Aqueous stock solution
160 mg/ml of *Uvariodendron kirkii* extract was prepared by weighing 1600 mg of freeze-dried extract and reconstituting with 10 millilitres of distilled water. Similarly, stock solution of 80, 40 and 20 mg / ml dose levels were prepared through double dilutions of the stock solution (Kaingu *et al*., 2012).

Experimental Animals
Female Wistar rats aged 10 - 12 weeks old and weighing between 180-220 grams were used. They were kept in cages (5 per cage), in an air-conditioned room at 22 ± 2oC and 60-70% relative humidity. Cages contained untreated wood shavings as beddings which were changed every other day. The animals were exposed to 12 hours light and 12 hours dark cycle, fed with commercial rat pellets (Unga Feeds Limited, Kenya) and had free access to clean water *ad libitum* (Bozcheloei *et al*., 2017). All the rats were handled humanely in accordance with the institution's Faculty of Veterinary Medicine Biosafety, Animal Use and Ethics Committee (FVM BAUEC/2019/190) guidelines and allowed to acclimatize for one week before study onset.

Experimental design
A completely randomized design was adopted. Female laboratory inbred Wistar rats, from the Department of Biochemistry, University of Nairobi, were used. Five rats were used for positive control (oxytocin). Five rats for each extract concentration (20, 40, 80, and 160 mg/ml), 5 rats for prostaglandin induced concentration and 5 rats for oxytocin induced contractions.

Preparation of the uterine tissues
Non-pregnant female rats were used and their oestrus cyclicity was closely monitored daily between 9 and 10 a.m. for about 15 days. Vaginal smears were collected, and slides observed under a light microscope in order to ascertain the oestrus stage (Marcondes *et al*., 2002). Rats in proestrus and oestrus stages of the oestrus cycle were selected as this is when the uterus is more receptive to contractility. One of the mechanisms that successfully deliver sperm to the fallopian tubes. In order to increase uterine sensitivity to contractile agents, the rats were injected with 2 mg/kg diethylstilbestrol subcutaneously 24 hours prior to study onset (Misonge *et al*., 2014). The rats were then humanely sacrificed using diethyl ether (Goodies *et al*., 2015). The uterine horns were immediately harvested and placed into a Petri dish containing previously warmed and aerated de Jalon solution. The uterine tissues were excised of all connective tissue. The uterine horns were cut into 2 cm strips (Watcho *et al*., 2010) and each strip was mounted in an organ bath containing 20 ml de Jalon's solution (Pakoussi *et al*., 2015; Kaingu *et al*., 2012).

De Jalon solution was maintained at a temperature of 37 ± 0.50°C and continuously bubbled with a mixture of 95% oxygen and 5% carbon dioxide (Misonge *et al*., 2014). Each uterine strip was mounted vertically within an organ bath. The upper end of the segment was hooked to an isometric force transducer (ML500/A, AD Instrument) coupled with Power Lab data acquisition system (Power Lab 8/30). The frequency of contraction (number of peaks recorded) and amplitude of contraction (in microvolts) were recorded and analysed using Chart5 software for windows.

Positive control contractions.
Non-pregnant uterine strips were harvested and prepared as described above. They were mounted and allowed (one at a time) to equilibrate for 30 minutes in de Jalon solution alone, after which its contractions were recorded for 10 minutes. These initial contractions were taken as the negative control recordings. After 10 minutes of negative control contractions the tissue was exposed to 1.0 ml Oxytocin which contained 10 IU synthetic oxytocin (Bafor *et al*., 2017). The isometric contractions were recorded for 10 minutes (taken as positive control), Frequency (rate) and amplitude (force) of uterine contractions was analysed from the chart recordings. Frequency was taken as the number of contractions recorded over the 10-minute period, that is, the number of peaks recorded. The amplitude or force was taken as the mean height in microvolts (μV) of the peaks produced over the 10-minute period. By comparing the frequency and amplitude of contraction for the control and test groups one was able to determine whether the extract increased, reduced or did not cause any effect in terms of frequency and amplitude of uterine contraction.

Effect of *Uvariodendron kirkii* aqueous extracts on non-pregnant isolated rats' uteri
Fresh uterine horns were prepared as previously described. Non-pregnant uterine tissue mounting was done. Soon after the first 10 minutes of negative control contractions, the tissue was exposed to 1 ml of 20 mg/ml *Uvariodendron kirkii* aqueous extract. The extract concentration was added to the organ bath inner chamber (containing de Jalon solution). Isometric contractions were recorded for 10 minutes, after which fresh de Jalon solution was used to wash the organ chamber before mounting a fresh uterine strip, which was exposed to 40 mg/ml extract concentration (Kaingu *et al*., 2012). The process was repeated using 80 and 160 mg/ml. Each extract concentration challenge was carried out using five rats. Frequency and amplitude of uterine contraction was calculated and recorded.

The effect of *Uvariodendron kirkii* aqueous extracts on oxytocin induced uterine contractions
Fresh uterine tissues were prepared. The tissue was mounted, one at a time, and after 10 minutes of negative control contractions was exposed to 1.0 ml oxytocin (containing 10 IU synthetic oxytocin). The isometric contractions were recorded for 10 minutes (taken as positive control), after which the strip was not rinsed and organ bath contents not altered. The uterine strip was thereafter exposed to 1 ml of 20 mg/ml of *Uvariodendron kirkii* aqueous extract and isometric contractions recorded for 10 minutes. The extract concentration was added into the organ bath inner chamber. The process was repeated 5 more times using fresh strips (Bafor *et al*., 2017; 2018). Similarly, fresh uterine strips were exposed to 40, 80 and 160 mg/ml extract concentration challenge. Frequency and amplitude of uterine contraction was calculated and recorded as previously described.

The effect of *Uvariodendron kirkii* aqueous extracts on prostaglandin induced uterine contractions
The above procedure was repeated using 1.0 ml prostaglandin F2α which contained 250 μg active ingredient, cloprostenol.

Data analysis
All values were expressed as percentage increase or decrease in mean ± standard error of mean (SEM) relative to the controls, using the following formula.

$$\%\ contractions = \frac{frequency\ or\ amplitude\ after\ treatment - control\ contractions}{control\ contractions} * 100$$

GraphPad prism 8.0.1(244) was used to analyse the data, that is

frequency and amplitude of uterine contractions using one-way ANOVA. P-values ($P < 0.05$ *; $P < 0.01$** and $P < 0.001$***) was considered significant. A post hoc Tukey's multiple comparison test was conducted to analyse statistical differences among groups.

Positive control

The data is expressed as mean ± standard error of mean (SEM) as a percentage increase or decrease in contraction frequency and amplitude relative to the control. Upon addition of 1ml of oxytocin the frequency and amplitude of contraction increased by 11.29 ± 0.774 % and 18.48 ± 4.363 % respectively, compared to the negative control with DE Jalon solution only.

RESULTS

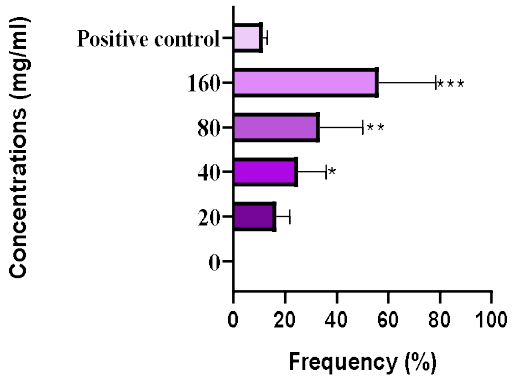

Fig.1A Effect of *Uvariodendron kirkii* extract on isolated uterine frequency of contraction.

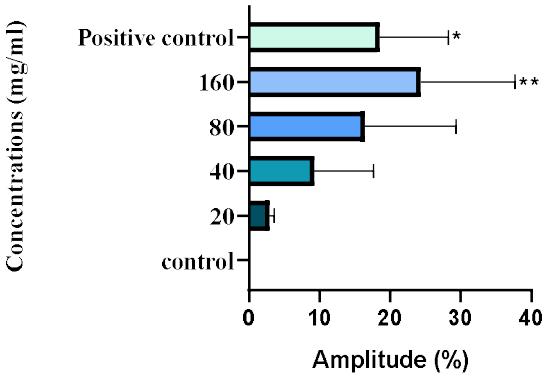

Fig.1B Effect of *Uvariodendron kirkii* extract on isolated uterine amplitude of contraction.

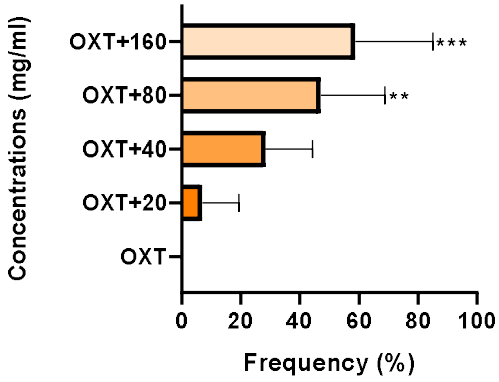

Fig.2A The effect of *Uvariodendron kirkii* extract on frequency of oxytocin induced uterine contractions.

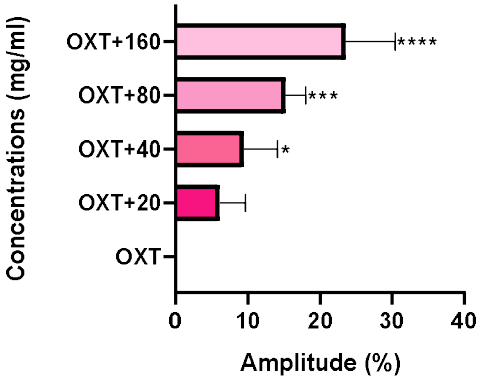

Fig.2B Effect of *Uvariodendron kirkii* extract concentrations on amplitude of oxytocin induced uterine contractions.

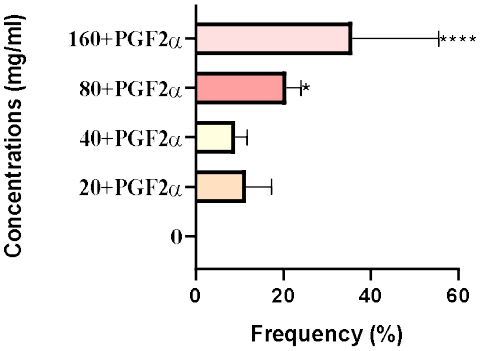

Fig.3A The effect of *Uvariodendron kirkii* extract on frequency of prostaglandin induced uterine contractions.

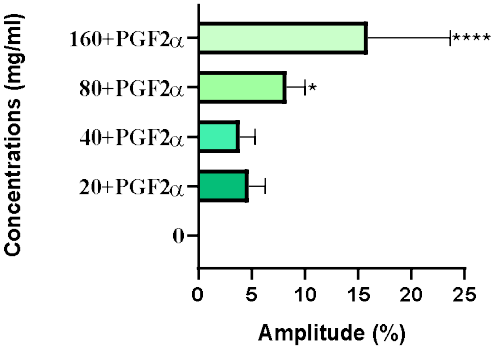

Fig.3B The effect of *Uvariodendron kirkii* extract concentrations on amplitude of prostaglandin induced uterine contractions.

Effect of *Uvariodendron kirkii* aqueous extract on frequency and amplitude of uterine contraction

Figure 1A and 1B represent the effect of *Uvariodendron kirkii* extracts on uterine frequency and amplitude of contraction. Upon addition of 20 mg/ml of the extract, the uterine contraction frequency increased by 16.53 ± 2.4 %, 25.12 ± 4.88 % at 40 mg/ml; 33.48 ± 7.37 % at 80 mg/ml and 56.39 ± 9.82 % at 160 mg/ml. The mean uterine contraction frequencies were significant ($p<0.05$) at 40 mg/ml, ($p< 0.01$) at 80 mg/ml and ($p< 0.0001$) at 160 mg/ml. Upon addition of 20, 40 and 80 mg/ml *Uvariodendron kirkii* extract, the amplitude increased by 2.87 ± 0.333 %, 9.22 ± 3.779 % and 16.37 ± 5.802 % respectively. 20, 40 and 80 mg/ml *Uvariodendron kirkii* extract concentrations caused a non-significant difference in amplitude of uterine contractions at ($p<0.05$). However, at 160 mg/ml, there was a significant ($p<0.01$) difference in amplitude of contraction, as the amplitude increased by 24.32 ± 5.997 % compared to the control. There was no significant difference in frequency of uterine contractions at 20, 40 and 80 mg/ml, and oxytocin (positive control) at ($p < 0.05$). However, there was a significant difference in frequency of uterine contractions between 160 mg/ml *Uvariodendron kirkii* extract and oxytocin at $p<0.0001$. The was a non-significant difference in amplitude of uterine contractions in all *Uvariodendron kirkii* extract concentrations and oxytocin at $p<0.05$ level of significance.

Effect of *Uvariodendron kirkii* aqueous extract on frequency and amplitude of oxytocin- induced uterine contraction

Figure 2A and 2B represent the effect of *Uvariodendron kirkii* extracts on oxytocin induced uterine frequency and amplitude of contraction. Oxytocin frequency and amplitude of uterine contraction was taken as control. The uterine contraction frequency increased by 6.92 ± 5.582 % at 20 mg/ml, 28.31 ± 7.193 % at 40 mg/ml, 47.06 ± 9.684% at 80 mg/ml and 58.78 ± 11.75 % at 160 mg/ml. The significance difference was at ($p<0.01$) at 80 mg/ml and ($p< 0.001$) at 160 mg/ml. At 20, 40, 80 and 160 mg/ml *Uvariodendron kirkii* respectively the mean amplitude of uterine contraction increased by 6.07 ± 1.617 %; 9.40 ± 2.087 %; 15.19 ± 1.250 % and 23.56 ± 3.096 % respectively. The increase in amplitude was significant ($p<0.05$) at 40 mg/ml, ($p<0.001$) at 80 mg/ml and ($p< 0.0001$) at 160 mg/ml.

Effect of *Uvariodendron kirkii* aqueous extract on prostaglandin-induced uterine contraction

Figure 3A and 3B show representatives on frequency and amplitude of prostaglandin induced uterine contractions. Prostaglandin frequency and amplitude of uterine contraction was taken as control. The percentage increase in frequency of uterine contraction was 11.44 ± 2.626 % at 20 mg/ml, 8.916 ± 1.257% at 40 mg/ml, 20.65 ± 1.462 % at 80 mg/ml and 35.71 ± 8.821 % at 160 mg/ml. There was a significant difference ($p< 0.05$) at 80 mg/ml and ($p< 0.0001$) at 160 mg/ml. The mean amplitude uterine contractions increased by 4.75 ± 0.694 % at 20 mg/ml, 3.89 ± 0.639 % at 40 mg/ml, 8.29 ± 0.766 % at 80 mg/ml and 15.91 ± 3.46 % at 160 mg/ml. There was significant difference ($p< 0.05$) at 80 mg/ml and ($p< 0.0001$) at 160 mg/ml.

DISCUSSION

Effect of *Uvariodendron kirkii* extract on uterine smooth muscle

The most significant finding of this study was the increase in frequency (rate) and amplitude (force) of uterine contractions caused by graded concentrations of *Uvariodendron kirkii* aqueous extract, as shown in Figures 1A and 1B. The plant has been used in Tana River county to expel the placenta, as a contraceptive and also as an abortifacient. The root bark is boiled in water and the decoction taken orally daily for the fertility regulation and the leaves are inserted in the womb after delivery to expel the placenta.

Other plants have been reported to have similar effects like *Uvariodendron kirkii* on the uterus. For instance, Ahangarpour *et al.,* (2010) reported that aqueous extract of *Cassia italica* leaves increased uterine contractions in rats, with the highest doses of the extract having the most contractile effect on the peak and frequency of uterus contraction. Another study by Kaingu *et al.,* (2012), reported that aqueous extracts of *Euclea divinorum* and *Ricinus communis* enhanced uterine contractility directly. Pakoussi *et al.,* (2018), also reported *Spondias mombin* leaves extract induced a spontaneous increase in uterine contraction amplitude by inducing prostaglandins release. Bafor *et al.,* (2009) also found out that the aqueous extract of the leaves of *Ficus exasperata* increased the frequency of rhythmic uterine contractions in Sprague-Dawley Rats, thereby justifying its use in easing of childbirth.

Nikolajsen *et al.,* (2011), have reported several Tanzanian plants to have induced strong and frequent uterine contractions in Sprague-Dawley Rats. The plants that increased both the force and frequncy of uterine contractions included *Bidens pilosa, Commelina africana, Desmodium barbatum, Manihot esculenta, Ocimum suave, Oldenlandia corym- bosa, Sphaerogyne latifolia, Obetia radula, Rubia cordifolia,* and *Triumfetta microphylla.* Ibrahim *et al.,* (2018), reported that the intensity of the contractions in presence of *Ficus deltoidea* var. Angustifolia aqueous extract increased moderately following the administration of the extract in a dose-dependent manner which is similar to this study. These results support their traditional claim of use of the plants in assisting labour, improving menstrual circulation, removal of retained placenta and treating post-partum hemorrhage.

The effect of *Uvariodendron kirkii* on uterine contractions can be explored in terms of treating or managing retained placenta as one of the causes is failed uterine contractions by the retroplacental myometrium (Urner *et al.,* 2014). Retained placenta is defined as failure of the foetal placenta (tufts) to separate from the maternal placenta (crypts). It is a serious problem in dairy cattle as is the main cause of cattle infertility and decreased milk yield (Zubair and Ahmad, 2014). Several studies have reported the use of medicinal plants in expelling retained placenta in cattle. The leaves of *Vernonia amygdalia* has been used to treat retained placenta by mixing with table salt, then administered to cow orally, and after some time the animal is relieved from retained placenta (Birhanu and Abera, 2015; Tekle, 2014).

The action of chemical extract from *Vernonia amygdalia* act as increasing uterine contraction by decreasing progesterone concentration, this increment of uterine contraction enhance removal of retained placenta (Yeap *et al.,* 2010). The chemicals such as tannins and flavonoids contained in the extracts of uterotonic plants act as antioxidants, antimicrobial and initiates the contractility of the uterus, thus placenta is easily detached and removed from the uterus (Abdisa, 2018). Tannin for instance produced by the plant has an astringent property that act by shrinking the small blood vessels which in turn lessens the capillary pressure and in turn lead to separation of the foetal membranes from the uterus (Amiera *et al*., 2014).

Flavonoids on the other hand has antioxidant properties and also assist in oestrogen activation. Oestrogen production leads to activation of contraction proteins, connexins, which in turn aid in placenta removal by increasing uterine contractions (Abdisa, 2018). A study by Kenana *et al*., (2019) on phytochemical analysis showed *Uvariodendron kirkii* to contain flavonoids in high concentrations and tannins which may cause the uterine contractility and therefore may aid in the removal of the placenta.

A study on *Ricinus communis* has suggested its use to treat retained foetal membranes (Birhanu and Abera, 2015). Other plants that have been suggested by the traditional medical practitioners for treating retained foetal membrane include: the leaves of *Ensete ventricosum* which are given to cattle during parturition (Mesfin *et al*., 2016). *Grewia ferrugina* extracts are useful for ease of expulsion of the placenta (Yadav *et al*., 2014). Bamboo leaves *Bambusa vulgaris* used together with black pepper *Qunda barbaree* assists in placenta expulsion (Abdisa, 2018). Raspberry leaves when consumed during the last 45 days of gestation period have low chances of development of peri-parturient diseases that is, prolonged labour and retained placenta (Simpson *et al*., 2001). Whole 100g of *Argemone mexicana* plant when used in feeds together with any available local grass once a day can be used for removal of retained placenta in cows (Yadav *et al*., 2014). Leaves of both *Opuntiieficus indica* and *Urera hypselodendron* are used for expulsion of retained placenta. The leaves are chopped, then mixed with water and administered to the animal orally (Bobaso *et al*., 2019). *Achyranthes aspera L.* has been reported to be used by people of Kalahindi district, Orissa, India, where the plant is applied on the genital part and also through inhalation to aid removal of the placenta (Sadangi and Sahu, 2004).

However, (Kaaria *et al*., 2019) reported that *Asparagus racemosus* caused a relaxation instead of uterine contraction. Similarly, (Pio *et al*., 2019) showed that *Rhaphiodon echinus* (Re) Crude Ethanol Extract, Lyophilized-Re and Hexane-Re relaxed utero fragment rats, pre-contracted in presence of potassium ions with concentration-dependent response. *Echinophora platyloba* and peppermint oil are reported to reduce uterine contractions. Peppermint oil antispasmodic effect on uterine muscle is by blockage of the calcium channels (Bahmani *et al*., 2015). Kauser *et al*., (2016), also reviewed on *Saraca asoka* bark and reported that it is used as a uterine tonic drug where it treats disorders associated with dysmenorrhea, abnormal bleeding, menorrhagia and threatened abortion.

Effect of extract on oxytocin and prostaglandin F2α induced uterine contractions

Physiologically, during labour and the immediate post-partum period, levels of oxytocin and prostaglandins are high within the uterus. During parturition, the levels of Oxytocin and prostaglandin gradually increase to facilitate parturition (Kaingu *et al*., 2012). The findings of the present study also showed that *Uvariodendron kirkii* increased the rate and force of Oxytocin induced uterine contractions as shown in Figures 2A and 2B. *Uvariodendron kirkii* graded contractions also increased the rate and force of prostaglandin induced uterine contractions as shown in Figures 3A and 3B.These findings corroborate those of Katuura *et al*., (2018), who reported that leaf extracts of *Vernonia amygdalina, Maesa lanceolata* and *Rhus natalensis* caused high frequency and amplitude of contractility in isolated rabbit uterus strips similar to, and in most cases higher, than that observed in oxytocin alone. Similarly, Eze *et al*., (2016) reported that addition of increasing concentrations of oxytocin in the presence of 80 mg ml/ aqueous extract of *Sida acuta* produced significant highest uterine contraction response compared to oxytocin and extract alone which is similar to the response stimulated by *Globimetula braunii* extract as studied by Ie and Zam, (2008). Both the plants potentiated the effect of oxytocin, which is similar to this study.

Oxytocin enhance uterine contractions by two main mode of action in the uterus. One, oxytocin binds to the myometrium oxytocin receptor to produce contractions and two, it binds to endometrium oxytocin receptor to increase prostaglandin production (Amiera *et al.,* 2014). Once oxytocin is stimulated, there is a markedly increase in intracellular concentrations of calcium ions and inositol triphosphate. The release of calcium ions stimulates calcium dependent calmodulin which activates the myosin light chain kinase which in turn catalyzes the contraction response (Arrowsmith and Wray, 2014). PGF2α on the other hand is produced by the uterine decidual cells. It enhances parturition by induction of luteolysis via the F prostanoids receptors (FP) in the luteal cells. Luteolysis results in cessation of progesterone production and luteal cell apoptosis. A decrease in levels of progesterone leads to the expression of the myometrium genes required for successful parturition (Sugimoto *et al.,* 2015).

This study is also corroborated by Kaingu *et al.,* (2012) where aqueous *Euclea divinorum* and *Ricinus communis* aqueous extracts enhanced prostaglandin and oxytocin induced uterine contractility. *Vitex doniana* bark aqueous extract induced graded uterine contractions and potentiated the effects of prostaglandins, ergometrine and oxytocin (Ladeji *et al.,* 2005). *Trichosanthes kirilowii* (Maxim.) root extract also similarly strengthened spontaneous contractions and enhanced response of uterus muscle to prostaglandin F2α and that of oxytocin (Gruber and Brien, 2011). Similarly, in this study *Uvariodendron kirkii* potentiated prostaglandin and oxytocin induced contractions as shown in figures 2A, 2B, 3A and 3B.

However, PGF2α induced uterine contractions were significantly reduced by ginger oil (*Zingiber officinale*) as shown by (Buddhakala *et al*., 2008). Other species of plants that have shown smooth muscle relaxation effect with anti-prostaglandin effect under laboratory conditions include *Citrus orantiifolia, Rosmarinus officinalis* and *Psidium guajava* (Andel *et al*., 2014). *Echinophora platyloba* is reported to reduce uterine contractions (Bahmani *et al*., 2015). *Foeniculum vulgare* inhibited prostaglandins induced uterine contraction (Mirabi *et al*., 2014).

Uterotonic plants can also be used to prevent or treat postpartum haemorrhage (PPH) (Gruber and Brien, 2011). As earlier stated PPH is caused mainly by uterine atony, and therefore conservative management techniques such as use of uterotonic medications are used as the first line of therapy. This is done to counteract uterine atony and therefore assist in retained placenta expulsion and removal of blood clots. One of the commonly used uterotonic is oxytocin (Likis *et al*., 2015). This study suggests *Uvariodendron kirkii* to be a uterotonic agent similar to oxytocin and therefore suggests its use in treatment of PPH.

Attah *et al*., (2012), suggests use of *Commelina africana, Vernonia amygdalina, Sida corymbose, Ocimum gratissimum, Hyptis suaveolens, Duranta repens, Calotropis procera, Sclerocarya birrea,* and *Saba comorensis* in treatment of PPH. *Commelina africana, Vernonia amygdalina* and *Sida corymbose* however yielded the biggest increase in uterine contractility in a pharmacological uterine model. The pharmacological results are in agreement with our results as *Uvariodendron kirkii* aqueous extracts increased uterine contractility. It is therefore of vital

importance to pursue alternative source of remedies for labour management.

CONCLUSION

In conclusion *Uvariodendron kirkii* root bark possess contractile effects towards isolated rats' uteri. The contractile effect of the plant explains its use in treatment of retained placenta and postpartum haemorrhage by women in Tana River county. The determination of uterotonic activity of crude extract of *Uvariodendron kirkii* provide a starting point towards its potential use in human as a natural source of uterotonic agent.

RECOMMENDATIONS

Further studies should be carried out to elucidate *Uvariodendron kirkii* mechanism of action in the uterus. It would also be important to isolate phytochemical compounds responsible for its uterotonic effect. Use of collagen gel uterine contractility assays to study the long-lasting uterotonic effect of *Uvariodendron kirkii* extract is also recommended.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

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