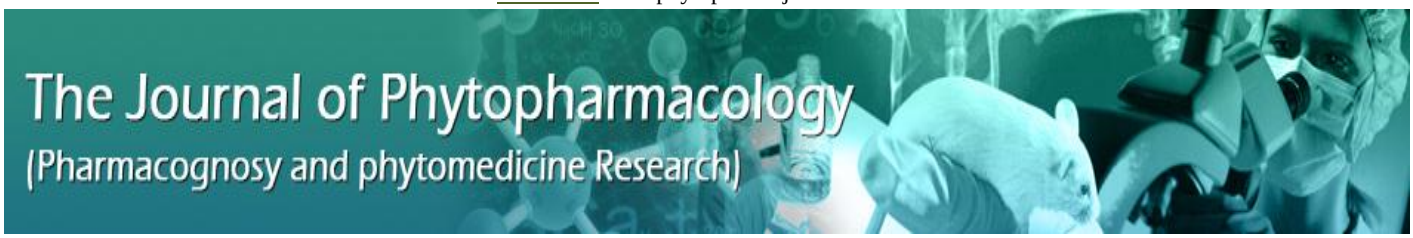
The Journal of Phytopharmacology 2015; 4(3): 190-196
Online at: www.phytopharmajournal.com



Review Article

ISSN 2230-480X
JPHYTO 2015; 4(3): 190-196
May- June

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A Review on Herbs with Uterotonic Property

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Abstract

The practice of herbalism has become popularized throughout the world. During past decade public interest in natural therapies is increasing both in developing as well as developed countries. Approximately 25 percent of all prescription drugs are derived from trees, shrubs or herbs. Plant-extract-based medicine is quite appreciated and well accepted by rural and even urban population. Uterotonics plants are those plants which have the ability to contract uterus and since ancient times these uterotonic plants have been used to assist labour, induce labour and for abortifacient purposes. Current available uterotonics include oxytocin, ergot derivatives and prostaglandins. Alternative to these synthetic agents, many herbal plants with uterotonic properties are known from across the world. For this purpose computerised databases were searched to get the various plant species which have been studied for their uterotonic activity. The aim of this review is to give snapshot of plants with uterotonic properties proved by experimental studies. More studies needed to prove them as uterotonic herbs. Before the assessment of clinical efficacy, studies must first provide evidence for the mechanism of action of herbs as uterotonics as well as their safety through phytochemical and pharmacokinetic assays.

Keywords: Uterotonics, Herbs, Contraction, Labour.

Introduction

The use of herbal drugs continues to expand rapidly across the world with many people now resorting to these products for treatment of various health related problems in different health care settings. During past decade the acceptance and public interest in natural therapies is increasing both in developing as well as developed countries.[1] Uterotonic is a substance that causes uterine contraction. In both allopathic as well as traditional system of medicine, uterotonic substances often have laxative, purgative, diarrheagenic, cathartic, abortifacient, and emmenagoguic properties.[2] Uterine stimulants are those medicines given to cause contraction of uterus, or to increase the frequency and intensity of the uterine contractions. Because of the property of causing uterine contraction, these drugs are used to induce or augment labour; facilitate uterine contractions following a miscarriage to reduce haemorrhage; induce abortion; or to prevent post partum haemorrhage. The three most frequently used uterotonics are the oxytocin, prostaglandins and ergot alkaloids.[3] Oxytocin is a biochemically synthesized hormone and act on distant hormone receptors to induce uterine contractions.[2]

In the developing countries, despite the availability of modern medicine, many people still rely on traditional healers and medicinal plants to meet their primary healthcare needs and that of their domestic animals.[4] Plant-extract-based medicine is appreciated and culturally well accepted by rural and even urban population.[5] Today in many countries modern medicine has replaced herbal medicine with many synthetic products.[6] The effectiveness of herbal medicine to cure various ailments is well proven. Their use promotes the development of modern therapeutics.[5] The aim of this review is to give snapshot of plants with uterotonic properties proved by experimental study.

Material and Methods: To collect the data various computerised databases were searched like pubmed, pubmed central, google scholar, medline, science direct with the keywords uterotonic, herbs, experimental study, herbal uterotonics, uetine stimulant, uterine contraction, labour induction, abortifacient.

Results: Researchers were able found sixteen plant species from all over the world which has been studied for their uterotonic activity either In vivo or In vitro model (Table1).

1. *Nymphaea alba* (Nymphaeaceae): Commonly known as the European White Waterlily, White Lotus, or Nenuphar and Kumuda in Sanskrit is an aquatic flowering plant of the family Nymphaeaceae,[7,8] globally distributed in Europe, North Africa, South West Asia, India, China and Russia.[7] It grows in water from 30-150 cm deep in large ponds and lakes. The diameter of leaves may be up to 30 cm. and spread in water around 150 cm per plant. The flowers are white in colour and have many small stamens inside.[8] The plant is found to contain tannic acid, gallic acid, alkaloids, sterols, flavonoids, glycosides,

hydrolyzable tannins and high-molecular weight polyphenolic compounds.[7,8] The ethanol extract of N. alba produced a dose related increase in the force of uterine contraction similar to Oxytocin. [9]

Figure 1: *Nymphaea alba*

Table 1: List of Plants studied for Uterotonic activity

S. No.	Botanical Name	Family	Part Studied
1	*Nymphaea alba*	Nymphaeaceae	Rhizome
2	*Raphanus sativus*	Brassicaceae	Leaf
3	*Carica papaya*	Caricaceae	Unripe Fruit
4	*Ficus deltidea*	Moraceae	Leaves
5	*Ficus asperifolia*	Moraceae	Fruit
6	*Gloriosa superb*	Liliacae	Root
7	*Jussiaea repen*	Onagraceae	Whole (except root)
8	*Agapanthus africanus*	Liliaceae	Leaf
9	*Harpagophytum procumbens*	Pedaliaceae	Root
10	*Caesalpinia bonduc*	Caesalpiniaceae	Leaf
11	*Clivia miniata*	Amaryllidaceae	Leaf
12	*Ekebergia capensis*	Meliaceae	Wood
13	*Rhoicissus tridentate*	Vitaceae	All parts
14	*Sesamum radiatum*	Pedaliaceae	Leaf
15	*Byrsocarpus coccineus*	Connaraceae	Leaf
16	*Monechma ciliatum*	Acanthaceae	Leaf

2. *Raphanus sativus* (Brassicaceae): The Raphanus is a Greek word which means 'quickly appearing' and refers to the rapid germination of plants belongs to this genus. It is commonly known as 'radish' which is derived from Latin radix (root), is an edible root vegetable grown and used throughout the world. Radishes are rich in ascorbic acid, folic acid, potassium and are considered as a rich source of vitamin B, magnesium, copper and calcium. They are found to contain low saturated fat and are very low Cholesterol.[10] The root's juice showed antimicrobial property. Aqueous extract of the roots showed antimutagenic effect against *Salmonella typhimurium*.[11] Study reports the gastrointestinal and uterine tone modulatory activities of the crude extract of radish leaves. Crude extract of radish leaves, shows the presence of saponins and alkaloids, exhibited spasmogenic effect (0.03-10 mg/mL) in isolated rabbit jejunum, rat stomach fundus and uterus which was partially blocked by atropine.[12]

3. *Carica papaya* (Caricaceae): Commonly known as the papaya pear, found in most tropical and subtropical countries of the world. It is a small tree with single stem which grows from 5 to 10m tall. The leaves are large with 50-70cm diameter, deeply palmate lobed with 7 lobes. The papaya plants are now cultivated at commercial level as a fruit crop in many countries.[13] Papaya found to contain polysaccharides, vitamins, minerals, enzymes, proteins, alkaloids, glycosides, fats and oils, lactins, saponins, flavonoids, sterols, etc.[14] The effect of aqueous extract of unripe Carica papaya was studied on isolated rat uterus and embryo. In the in vitro model, *Carica papaya* showed contractile effect on the isolated uterus in diestrus stage and when given orally in dose of 200 and 400mg/kg to pregnant rats, resulted in gradual decrease in body weight indicating embryonic resorption.[3]

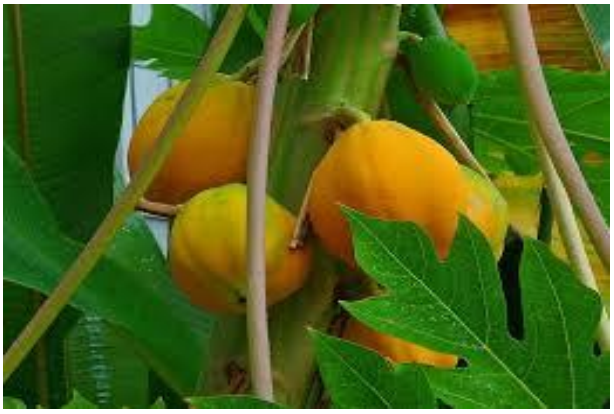

Figure 3: *Carica papaya*

4. *Ficus deltoidea* (Moraceae): It is a traditional medicinal plant widely distributed in Southeast Asia.[15] In Malaysia, it is known as "mas cotek".[15,16] Toxicological study on *F. deltoidea* showed that the plant does not contain toxic components.[17] The phytochemical constituents claimed to be present in *Ficus deltoidea* are the flavonoids, isovitexin, vitexin, proanthocyanidins, flavan-3-ol monomers and flavones glycosides.[16] *F. deltoidea* aqeous extract (FDA) induced in-vitro contraction of the isolated rat's uteri in a dose-dependent manner.[18]

Figure 4: *Ficus deltoidea*

5. *Ficus asperifolia* (Moraceae): It is an average or small size tree, terrestrial or epiphyte reach up to 20m in height. *F. asperifolia* is frequently found in the savannah regions, especially along river banks as well as marshy areas at an altitude of up to 1100m. It contains enormous leaves which displayed spirally, the limb is either oval or has a form of ellipse and the roots are often fibrous. It is one of the

highly important medicinal plants with a variety of uses such as analgesic, antitumor, anticancer, diuretic, abortificient and ecobolic.[19,20] The effects of aqueous and methanol extracts of the dried fruits of *F. asperifolia* were evaluated on estrogenized isolated rat uterus in the presence and absence of atropine, pyrilamine maleate, indomethacin or hexamethonium. Aqueous and methanol extracts as well as oxytocin, acetylcholine and histamine elicited concentration dependent contractions of the uterus. Atropine, pyrilamine maleate and indomethacin concentration dependently blocked the response of the uterus to acetylcholine, histamine and oxytocin, respectively, and to aqueous extract.[21]

Figure 5: *Ficus asperifolia*

6. *Gloriosa superb* Linn (Liliacae): It is an important medicinal plant which comes under endangered species among the medicinal plants. In Southern India it is called as glory lily and climbing lily-in English.[22] It is a native to tropical Africa, India and south-eastern Asia, now widely cultivated throughout the world as an ornamental plant. *G. superba* is a tuberous plant with V or L-shaped, finger like tubers that are pure white when young, becomes brown with age. It is a climbing herb, up to 6 m long, bearing pointed, dark green colour, glossy leaves, each equipped with a tendril by which it climbs onto other plants.[23] Seeds and tubers contain valuable alkaloids such as colchine and colchicoside, which are used as an antidote for snake bites, gout and rheumatism. Phytochemical study of the extract from the tuber and seed samples were yields high amount of various biologically active compounds as compared to leaves and flowers.[24] Uterotonic assessment *in-vitro* and *in-vivo* of aqueous extract of G. superba was carried out in rats. Oxytocin was used as the standard uterotonic. Both the oxytocin and the extract produced dose dependent contractions.[25]

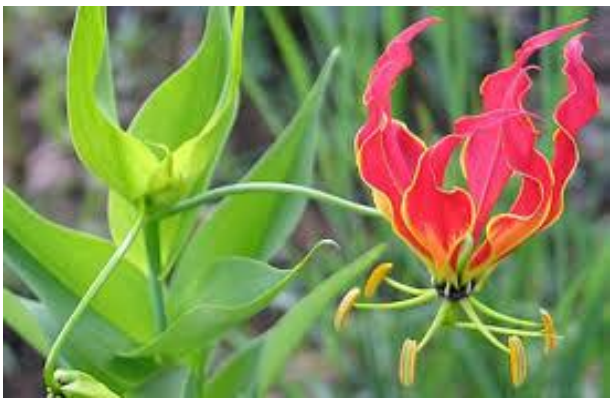

Figure 6: *Gloriosa superb*

7. *Jussiaea repens* (Onagraceae): Locally known as 'Kesardam' is a water creeping prime rose.[26] Its stem and leaves float on the surface of water and flowers consist of five white petals which are yellow at the base. It is a well known medicinal plant which has great medicinal values such as anti-diabetic, anti-inflammatory, hepatoprotective, antibacterial activities.[27] It is found in wetlands of different parts of India, China, Malaysia, New Guinea and other countries.[28] Different scientists reported that aerial parts of the plant is composed of various metabolites like, rutin, kaempferol, quercetrin, quercetin, terpenes, triterpenes etc.[29] One in-vitro study shows that the crude aqueous extract of Jussiaea repens causes significant increase of force and frequency of contraction than normal on isolated non pregnant uterus of adult female rats. The results (as percentage) was compared with the effect of oxytocin in presence of atropine (oxytocin blocker) which shows that the extract may act as oxytocin which is antagonized by atropine.[30]

Figure 7: *Jussiaea repens*

8. Agapanthus africanus (Liliaceae): The genus Agapanthus, a member of family Liliaceae, contains several ornamental species such as *A. afrleanus*. *A. ilsaperthus*, and *A. praeccx*. These species have flowers with dark blue-violet to milky white colors and commonly called 'agapanthus' or 'Iily of the Nile'.[31] Agapanthus roots are traditionally used by local communities in South Africa as medicine for various disorders. Infusions or decoctions of *A. africanus* are traditionally used by Xhosa women during pregnancy to induce labour. It is also frequently used for the treatment of constipation in pregnancy, as antenatal or post-natal treatment of the mother and also for high blood pressure.[32] The effect of an aqueous extract of *A. africanus* leaves was tested on the isolated rat uterus preparation. The extract of *A. africanus* leaves was found to exhibit agonist activity on uterine muscarinic receptors and to promote the synthesis of prostaglandins in the oestrogenized rat uterus.[33] Aqueous extracts of *A. africanus* and *C. miniata* leaves have been shown to possess similar uterotonic activities in the isolated whole uterus preparation. Both herbal extracts caused a direct contractile response by the isolated tissue. [34]

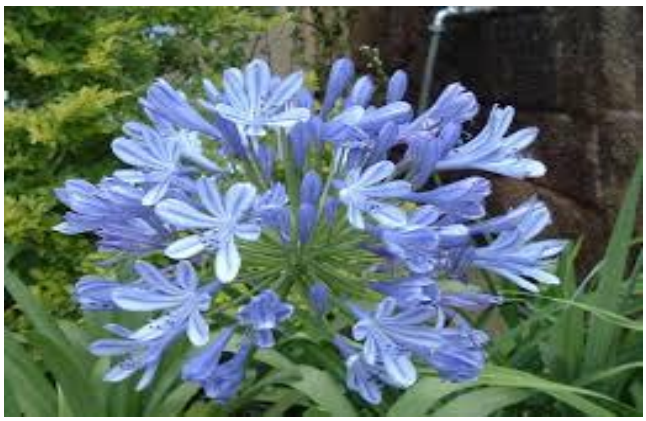

Figure 8: *Agapanthus africanus*

9. *Harpagophytum procumbens* (Pedaliaceae): Commonly known as Devil's Claw, is a herbaceous plant species which has the high level of medicinal use. It has historically been used to treat different ailments like fever, malaria, indigestion and pain.[35] The fruits are 7-20 centimeters long and 6 cm in diameter which contain approximately

50 dark seeds. The flowers are large, pale-pink to red. The part which is medicinally used are dried tubular and secondary roots as well as the macerated thick lateral tubers.[36] Secondary root aqueous extract (HPE) of *Harpagophytum procumbens* was studied on isolated uterine muscle strips of pregnant and non-pregnant, young female rats. The plant's extract increases in the baseline tone (basal tension), and caused powerful spontaneous, rhythmic, myogenic contractions of the oestrogen-dominated uterine muscle strips taken from stilboesterol-pretreated, non-pregnant female rats.[37]

Figure 9: *Harpagophytum procumbens*

10. *Caesalpinia bonduc* (Caesalpiniaceae): It is a wild highly thorny shrub commonly known as the Gray Nicker Bean. It is a free-flowering and free-fruiting plant without periodicity.[38] It is widely distributed all over the world specially in India, Sri Lanka and Andaman and Nicobar Islands. In India, it is specially found in tropical regions.[39] All parts of the plant is considered to have medicinal properties so it is a very important medicinal plant which is used in traditional system of medicine.[39,40] The leaf extract of *Caesalpinia bonduc* Roxb. was studied in isolated pregnant rat myometrium preparations. The extract of *Caesalpinia bonduc* increased the contractile force in the isolated strips in a concentration-dependent manner. The effects were comparable to those obtained with acetylcholine. Contractions induced by *Caesalpinia bonduc* or acetylcholine were inhibited in the presence of atropine.[41]

Figure 10: *Caesalpinia bonduc*

11. *Clivia miniata* (Amaryllidaceae): The genus Clivia is a group of perennial herbaceous plants.[42,43] The most commonly cultivated species is Clivia miniata Regel that is cultivated in many parts of the world, especially in Europe, the USA, Japan, China, Australia, New Zealand and Belgium. Boiling water extracts of *C. miniata* leaves were found to cause concentration-dependent contractions in both the isolated uterus and ileum.[42] Aqueous extracts of *A. africanus and C. miniata* leaves have been shown to possess similar uterotonic effect in the isolated whole uterus preparation. Both herbal extracts caused a direct contractile response by the isolated tissue. [41]

Figure 11: *Clivia miniata*

12. *Ekebergia capensis* (Meliaceae): It is evergreen tree, medium-sized to large, 7-20 meters tall and widely distributed in Africa.[44,45] E capensis extracts are used to relief heartburn, coughs and respiratory complaints, and decoctions made from the wood of this plant are used by the Zulus in KwaZulu-Natal as oxytocic agents.[45] The uterotonic properties of extracts from *Ekebergia capensis* were evaluated by using both pregnant and non-pregnant guinea pig uterine smooth muscle in vitro. The extracts were prepared by using water modified supercritical carbon dioxide at 400 atm and 80 degrees C. The results of this study show that two compounds from the extract of the tree possess varying degrees of agonist activity on uterine smooth muscle.[46]

Figure 12: *Ekebergia capensis*

13. *Rhoicissus tridentata*: It grows in bushy areas and develops underground tumors.[47] Decoctions of the roots and lignotubers of Rhoicissus tridentate are used by southern African women in ethnic herbal remedies for delayed childbirth and to facilitate childbirth. Isolated rat uterus tissue was used to compare the contractile activity of crude aqueous extracts of R. tridentate made from plant material harvested every 3 months over a period of 2 years. The activity of the plant extracts from those plants which are harvested in summer and autumn were 4-5 fold higher than extracts from those plants harvested in winter or spring. The tubers were found to stimulate the greatest degree of contractions, followed by the stems, roots and leaves.[48]

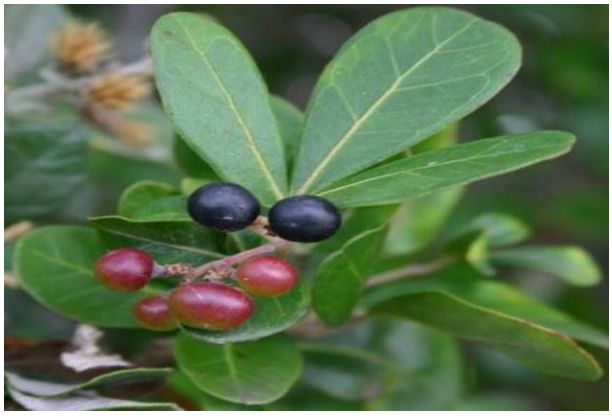

Figure 13: *Rhoicissus tridentata*

14. *Sesamum radiatum* (Pedaliaceae): It is a leafy vegetable belongs to the group of indigenous vegetable that grow in small quantity in the rural areas. It is one of the neglected leafy vegetables of the tropics despite its nutritional contribution. This plant occurs in the tropical Africa mainly as weed, where it is gathered in the wild and used as a potherb.[49] The effects of the aqueous leaf extract was examined on the contractile activity of uterine smooth muscle isolated from pregnant Wistar rats (19-21 days). *S. radiatum* aqueous leaf extracts (ESera, 1×10-4 µg/ml - 100µg/ml) showed uterotonic properties. These uterotonic effects were characterized by the increase of the amplitude, the frequency and the basal tone of the uterine smooth muscle strips in normal Mac Ewen solution and by the development of contracture in depolarizing solution and in solution without calcium. Similar effects were observed with Oxytocin (OT, 2.5×10-14µg/ml - 2.5×10-9 µg/ml) and misoprostol (Miso, 1×10-3 µg/ml – 0.08µg/ml).[50]

Figure 14: *Sesamum radiatum*

15. *Byrsocarpus coccineus* (Connaraceae): It is a shrub widely dispersed in tropical Africa, widely used in ethnomedicine for the treatment of various ailments like mouth and skin sores, swellings, tumors, earache, muscular and rheumatic pains, venereal diseases, jaundice, pile and dysentery. The plant extract has also been shown to possess oxytocic, antioxidant, antidiarrheal activities[51,52] *In-vivo* uterotonic effects of the ethylacetate leaf extract of *Byrsocarpus coccineus* in pregnant rat uterus was studied. Ethylacetate leaf extract of *Byrsocarpus coccineus* potentiated the delivery of pregnant rats on days 21 of pregnancy. The results of the abortificient effect of the ethyl acetate extract on the pregnant rats showed no significant difference between the treatment groups compared with the control ($p>0.05$).[6]

Figure 15: *Byrsocarpus coccineus*

16. *Monechma ciliatum* (Acanthaceae): It is a small herb grows a few inches above the ground, leaves measuring about 4-7 X 1–2 cm.[53] In Arabic language it is known as 'El-Mahlab, El-Aswad.[53,54] It was used in remedy to relief body pain, liver, cold, diarrhea and sterility in women.[54] The oxytocic activity of the hot methanol extract (HME) of the leaves of *Monechma ciliatum* was compared with other uterine stimulants like ergometrine, oxytocin, 5-hydroxytryptamine (5-HT), acetylcholine (ACh) and prostaglandins (PGs) E2 and F2alpha (PGE2 and PGF2alpha) in the presence of some antagonists in an attempt to explain the mechanism of action of the extract. Results suggest that the HME may be acting by more than one mechanism to contract the uterus and explains the mechanism of the anti-implantation activity of the plant.[55]

Figure 16: *Monechma ciliatum*

Conclusion

The above-mentioned sixteen herbs have been studied for their possible uterotonics effects. More experimental studies required to finally conclude all these as uterotonic herb and before the assessment of clinical efficacy, studies must needed first to provide evidence for the mechanism of action of herbs as uterotonics as well as their safety through phytochemical and pharmacokinetic assays.

Conflict of interest

None declared.

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