Review article

Traditional Medicines and Women Reproductive Health: An Alternative to Modern Synthetic Drugs

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Abstract: Medicinal plants are rich repository of phytocompounds having the properties to cure various ailments and play pivotal role in the maintenance of health especially among the indigenous people living with the nature. These people have been relying on traditional medicine both plant and animal origin since time immemorial as the modern medical facilities is not easily accessible. The indigenous people explore the nature and natural resources for their livelihood and they acquired tremendous knowledge on the medicinal properties of the natural products. The traditional medicines especially the medicinal plants used by the indigenous people are not only used to cure ailments but also to maintenance and regulation of reproductive health. Certain plant and plant products are used for regulation of women reproductive health by the indigenous tribal peoples around the globe. There are many medicinal plants used traditionally by the indigenous people that have efficacy to regulate reproductive system both in human and domestic animals. This ethno-medicinal information emerged from the age old traditional knowledge system leads to the development of new drugs with lesser or no side effects. Thus traditional medicine become the promising field for the scientists for developing new compounds for improving human health especially female reproductive health without the using synthetic drugs which have several significant side effects. The modern medical science developed and provides a number of synthetic compounds to regulate the reproductive health of women in the form of contraceptives and abortificants to avoid unintended pregnancy. However, these synthetic medicines have lots of side effects causing serious issues to the women health. Therefore, alternative traditional-based herbal formulation for reproduction regulation is the priority of scientific research during last few decades. In the present review, an attempt has been made to portray the importance of medicinal plants for reproductive health.

Key words: Contraceptive, Medicinal plants; Phytoestrogen, Reproductive Health, Traditional medicine

Introduction

Medicinal plants are rich repository of phytocompounds having the properties to cure various ailments and play pivotal role in the maintenance of health especially among the indigenous people living with the nature. These people has been rely on traditional medicine (TM) both plant and animal origin since time immemorial as the modern medical facilities are not

easily accessible. The indigenous people explore the nature and natural resources for their livelihood and they acquired tremendous knowledge on the medicinal properties of the natural products. These acquired indigenous knowledge gradually become the basic health care system among the indigenous society. They are using this traditional knowledge

system for the benefit and maintaining of human health. The traditional medicines especially the medicinal plants used by the indigenous people are not only used to cure ailments but also to maintenance and regulation of reproductive health. Certain plant and plant products are used for regulation of women reproductive health by the indigenous tribal peoples around the globe. There are many medicinal plants used traditionally by the indigenous people that have efficacy to regulate reproductive system both in human and domestic animals. These ethno-medicinal informations emerged from the age old traditional knowledge system leads to the development of new drugs with lesser or no side effects. Thus traditional medicine become the promising field for the scientists for developing new compounds for improving human health especially female reproductive health without the using synthetic drugs which have several significant side effects. The World Health Organization (WHO) also put emphasis on research on medicinal plants and established "The Task Force on Plants for Fertility Regulation" for identifying and selection of medicinal plants used for human reproduction regulation (Griffin, 1988). The objective of this mission is to formulate new herbal origin drugs to mitigate the female reproductive abnormalities which are a global concern in the modern human societies.

The role of women in the human civilization is indispensable. Women play an imperative role in the human society since the societal development on earth is directly related to the health status of the women. Thus, "women reproductive health" is one of the major concerns of the modern world. Traditionally, the health of a woman has been determined by maternal and reproductive health status measured with attaining of motherhood and other feminine physiological conditions. The reproductive physiology of women is very complex in comparison to men. During the life of an woman, there are a number of physiological events occur onset with menarche and culminates with menopause. The complete stages of pregnancy itself a very complicated process. Besides complicated reproductive physiology, a woman gone through many diseases and health care issues

in her life time including poor nutrition, stress, malnutrition and many reproductive abnormalities. The poor health status leads to the complicacy in pregnancy as well as causes deleterious effects on child. In addition to that consecutive pregnancy causes serious health issues to the mother. To get rid of this havoc, the rural women using various medicinal plants and plant products since time immemorial. The modern medical science developed and provides a number of synthetic compounds to regulate the reproductive health of women in the form of contraceptives and abortificants to avoid unintended pregnancy. However, these synthetic medicines have lots of side effects causing serious issues to the women health. Therefore, alternative traditional-based herbal formulation for reproduction regulation is the priority of scientific research during last few decades.

The physiology of female reproduction is tightly regulated by the gonadal hormones-estrogen and progesterone. The hormones estrogen and progesterone are endocrine chemical messengers; exert effect on target cells of different tissues elsewhere in the body (Guyton, 2006). These two hormones are the primary regulators of the reproductive functions of the female during the reproductive cycle and pregnancy. The modern contraceptive is based on the manipulation of status of these two hormones by introducing exogenous hormonal therapy as birth control device. One of the most popular birth control devices is the hormonal oral contraceptive used by the women all over the world. Yet, there are still numerous challenges in contraceptive development for fertility regulation and development of hormonal therapy with respect to reproductive health of women. Use of such hormonal therapies was reported to invite unknown complications and side effects to the womens' health (Williamson et al., 2009). These side effects may extend to the most adverse condition of the women's health generating endometrial carcinogen. Consequently, search for a new medicinal product still continues to improve and develop an effective and safe alternative to conventional hormonal therapy. Some other problems related to the reproductive health of women are anomalies of hormonal functions in their target

tissues. Imbalance of hormones causes many physiological problems that affect directly or indirectly women's health. The failure of the ovary to produce estrogen results in hot flashes, and/or sleep disturbances, accelerated bone loss, increased risk of colon cancer and weight gain. These effects have been accompanied by shifts in plasma lipoprotein, cholesterol profiles associated with a higher incidence of cardiovascular diseases (Hoffman and Zup, 2003), ovulation disorder, polycystic ovary syndrome (PCOS) (Doi *et al.*, 2005), abnormal cervical mucus, premature menopause etc. (Davis, 2001). Failure of hormonal synchronization is tackled with conventional hormone replacement therapy (HRT) replacing estrogen (Glazier and Bowman, 2001).

Phytotherapeutic management of endocrine dysfunctions allows hormone free choices for addressing conditions associated with PCOS (Joseph and Collins, 2006), menopause (Wanibuchi et al., 2003), breast cancer (Rice and Whitehead, 2006), endometrial carcinoma etc. (Wanibuchi et al., 2003). World Health Organisation (WHO) designed a draft strategy to the resolutions adapted by 55th World Health Assembly to improve reproductive health of women all over the world demanding reproductive health care and cure and prevention of sex related diseases (WHO, 2004). Understanding of the mechanism by which the plant-derived substances affect the biological system will allow individuals with more hormone-free options that significantly impact quality of life and risk of diseases. Following this principle of hormone free options a growing number of women turned to use herbal remedies to solve their feminine problems (Vikers et al., 2006; Holst et al., 2009). As desired, a specific drug should be effective enough to cause the purpose, physiologically safe with low toxicity without any side effects, reversible in action and easy to use. It has been speculated that herbs may fulfil the demand of such a safe and effective contraceptive and be the alternative to the synthetic hormonal therapy.

Many plants have been evaluated to develop a safe novel drug to be used for replacing conventional hormonal therapy including the contraceptive medicine. The plant possesses a kind of compound(s) that shows similar action of ovarian hormone particularly the estrogen in the estrogen responsive tissues. These substances are termed as 'phytoestrogen', interact with the estrogen receptors in the way the ovarian estrogen does in the cells of estrogen responsive tissue of reproductive organs and exerts effect similar to the estrogen. The uterine endometrium is the estrogen responsive tissue undergoing proliferation and differentiation under the influence of the ovarian estrogen. Similarly, administration of phytoestrogen induces the proliferation and differentiation of the uterine endometrium. Several phytoestrogens have been isolated so far and evaluated its estrogenic effects on both animal models and human being. Genistein, pueranin, diadzein, coumestrol etc. are some of the phytoestrogens isolated from various plants in recent years. With the ability to alter the hormonal status of the estrogen responsive tissue, these phytosteroids may disrupt the normal function of the reproductive organs. In contrast, many phytoestrogens have beneficial effects on prevention of cancer, maintenance of menopausal symptoms and bone mineral density, cardiovascular disease, obesity etc. (Usui, 2006; Ososki and Kennelly, 2003). Discovery of such non steroidal compound(s) may lead to development of a new health friendly drug as an alternative conventional hormonal contraceptive and alternative of hormone replacement therapy.

Non-steroidal drug development for reproduction regulation

The changing interest of developed and developing countries in the natural resources have opened a new horizon of drug development on the basis of traditional knowledge with the perspective of safety and efficacy. Medicinal plants are traditionally used for the reproductive health problems either as profertility or antifertility drug by the people of different societies all over the world. The knowledge on medicinal system prevails for centuries among the folk people of different part of the world. Very often, this indigenous knowledge are available as oral literature, while in the country like India these knowledge were scripted in the form of valuable ancient

literature e.g., Ayurveda. With the advancement of time and development of modern medical science, this traditional crude medicine of herbal origin has drawn attention of the scientific communities across the world. Various Governmental and non Governmental organizations all over the world initiated the process of documentation of these medicinal plants for human and animal welfare. In this regard the WHO plays a pivotal role in exploration, utilisation and protection of these traditional medicines exists among the people of various societies in the different countries. The WHO's "Traditional Medicine Strategy 2002-2005" dramatically increased the pace of research on herbal products among the scientists of the world community. On the basis of WHO special programme in search of herbal solution for female reproductive problems, research has been carried out in many developed and developing countries including United States, South Korea, England, China, India, Indonesia, Brazil, South Africa etc. for finding a new lead of herbal derivatives. As a result, a multitude of fertility regulatory phytocompounds have been reported from various countries of the world to address the female reproductive health problems and contraceptive medicines. China, the most populous country of the world has been brought with for the discovery of some compounds for fertility regulation in female. 'Yuehchukene' (YCK), an indole alkaloid has been isolated from the root of Chinese medicinal plant Murraya peniculata. However, the YCK was failed to develop as a antifertility drug as it showed low level of estrogenicity (Fabricant and farmsworth, 2001). Many other phytocompunds viz. 'Trichosanthin' and 'Yuanhuacine' having abortifacient properties have been isolated from Chinese medicinal plants Trichosanthes kirilowii and Daphne genkwa respectively (Lee, 2000). Studies in western medicinal system revealed use of plant products 'hyoscine' and 'ergometrine' having effects on uterus used for obstetrics and gynaecological problems (Philipson and Anderson, 1988).

Around seventy traditionally used Ethiopian plants subjected to uterotonic and antiimplantation bioassays have been reported with antifertility activity (Belachew, 1994). Similarly, *Pelago Indians* of Argentina have tradition of using

herbal drugs with antireproductive activity (Fillipov, 1994). Two marine red algae viz., Gelidiella acerosa and Gracilaria corticata have been reported as the useful source of potential postcoital contraceptive drugs from Sri Lanka (Ratnasooriya et al., 1994; Premakumara et al., 1995). Dried leaves of Casia nigricans is used for family planning by the 'Rukuba' community of 'Jos metropolis' (Nwafor and Okwuasaba, 2001). A folk medicine 'Pergularia daemia' is used by the rural people of Bangladesh to induce abortion (Sadik et al., 2001). The Ethiopian herb Rumex steudelii (Gebrie et al., 2005) and Achyranthes aspera (Shibeshi et al., 2006) have been reported to possess antifertilty property in albino rats. An indigenous contraceptive herbal formulation consisting of a mixture of Lepidagathis longifolia, Palaquium sp. and Phyllagathis rotundifolia was used by the Temuan Aborigins of Malaysia (Islam et al., 2007). The uterolytic effect of traditional abortifacient medicine Hypoxis hemerocallidea of South Africa has been demonstrated. Changes in tension developed by the aqueous extract of the Hypoxis hemerocallidea, a traditional abortifacient medicine of South Africa, has been recorded by means of basile's force-displacement transducers and penwriting 'Gemini' recorders (Nyinawumuntu et al., 2008).

Caribbean folk medicines comprising a numbers of plants including Achyranthes indica, Coleus aromaticus, hibiscus rosa-sinensis, Scoparia dulsis with many other potent medicinl plants are used for curing reproductive problems in Trinidad and Tobago (Lans, 2007). The medicinal plant Aspilia Africana has the reputation for contraception among the 'Mbaise' and most 'Igbo' speaking parts of Nigeria (Oluyemi et al., 2007). Embryotoxic effect of Cissus sicyoides, popularly known by its antidiabetic action in Brazil has been reported to be embryotoxic in rats (Almeida et al., 2007). Embryotoxic property of another plant Acanthus montanus, used in folk medicine of Cameroon was observed in albino rats. The aqueous extract caused appreciable preimplantation loss and delayed fetal growth (Asongalem et al., 2008). A group of Europian scientists has recently reported that Rhaponticum carthomoides, a perennial herb used for centuries in eastern part of Russia exert effects on reproduction and sexual function

(Kokoska and Janovska, 2009). These plants tested in various laboratories of the world as mentioned above have furnished a strong background of ethnomedicinal knowledge in terms of feminine problems. Screening of such medicinal plants may provide information regarding non-steroid estrogenic compound(s) with the capabilities to manipulate ovarian estrogen with safety and efficacy to be used as an alternative to conventional hormonal therapy.

Herbal medicines for fertility regulation in Indian context

India is the rich repository of plant species with huge varieties of medicinal plants. The scientists of Indian subcontinent have reported a number of medicinal plants for fertility regulation during twentieth century. A multitude of Indian plants for unspecified anti-reproductive activity has been documented and mentioned in different literature during last few decades (Kirtikar and Basu, 1998; Chopra et al., 1956; Bhakuni et al., 1990; Dhawan et al., 1977; Garg et al., 1978; Prakash et al., 1976; Nath et al., 1992; Upadhyay et al., 1994). Antifertility properties of various plants like Piper longum, Lawsonia inermis, Abrus precatorius, Curcuma longa, Embelia ribe, Plumbago rosea , Hibiscus rosa sinensis, Ferula jaeschkeana, Azadiracta indica, Carica papaya, Moringa oleifera etc. have been reported by these authors. The dimension of this research has been increased and changed with the report of potential herbal derivatives and their target specific effects for fertility regulation by the beginning of 21st century.

Aqueous extract of seeds of Indian plant 'Cassia fistula' showed antiimplantation activity in female rats (Yadav and Jain, 1999). The 'bark' of an Indian herb 'Alangium salvifolium' showed antifertility effect in female wistar rats (Murugan et al., 2000). A composite root extract of five plants viz. Plumbago rosea, Dolichos lablab, Shorea robusta, Carica papaya and Cannabis sativa has been found to induce reversible sterility in albino rats effecting the ovarian follicle and endometrial surface epithelium (Sarma and Mahanta, 2000). The widely used rhizomes of turmeric Curcuma longa is a potential Indian traditional medicine for the development of a novel intravaginal contraceptive

(Chattopadhyay et al., 2004). The 'Curcumin' from the Curcuma longa has been reported to be a potential vaginal contraceptive (Rithaporn et al., 2003). Ethnomedicinal survey of the tribal areas of southern Rajasthan uncovered 53 plants belonging to 33 families which are used to cure sexual diseases and use for family planning (Jain et al., 2004). These studies illustrate the importance of different parts of the medicinal plants in curing reproductive health problems. The tribe 'Chenchus' living in the forest of Nnallamalais in Kurnool district of Andhra Pradesh, used the root of Pentanema indicum for abortion (Reddy et al., 2007). Pregnancy interceptive property of root extract of Melia azedarach (Keshri et al., 2003), and Calotropis gigantea (Srivastava et al., 2007) have shown in vivo in albino rats. Docking analysis of 'rohitokene' an alkaloid isolated from the active chloroform soluble fraction of bark of Dysoxylum binecteriferum showed contraceptive property. This study revealed that the 'rohitokine' with almost similar molecular size (MW 305kD) as estradiol-17â appears to fit ideally into the hydrophobic pocket of estrogen receptor (Keshri et al., 2007). The plant Wrightia tinctoria with ethnomedicinal background for various ailments found in Madhya Pradesh, Rajasthan, Tamilnadu has been reported for promising antifertility activity. A series of fractions prepared with non polar and polar solvent of bark of Wrightia tinctoria showed 100% anti implantation activity (Keshri et al., 2008).

India has the sufficient amount of information on the herbal contraceptive to define the status of herbal legacy in traditional knowledge system. There are still a large number of territory remained to be explored that may lead to discovery of new herbal solution for fertility regulation. The north east region of India being one of the richest zones of biodiversity gifted with majestic Himalayan range harbouring wide varieties of flora, has exceptionally higher potentiality in the medicinal plant sector (Kala *et al.*, 2006). The Government of India has set up the Traditional Knowledge Digital Library (TKDL) to protect Indian Traditional knowledge on various aspects including the Traditional Medicines. Data on 65,000 formulations in Ayurveda, 70,000 in Unani and 3,000 in Sidha had already been entered in TKDL.

The Polygonum hydropiper is mentioned in various literatures as a vegetable as well as medicinal plant for curing various ailments. The herb Polygonum hydropiper has long been used as a spice in Japan and China and it is one of the traditional vegetables in Japan (Miyazawa and Tamura, 2007). However, the phytochemistry of Polygonum hydropiper's root is still not clear. Traditional practice of using roots of this wild herb for termination of undesired pregnancy is still popular among groups of tribal people of Assam. The estrogenic property of the Polygonum hydropiper has been described in ovariectomized rats (Hazarika and Sarma, 2008). This property of the crude root extract of Polygonum hydropiper may be responsible for the follicular recruitment in the ovaries of cyclic rats (Hazarika and Sarma, 2006). These findings led to the chromatographic fractionation of the methanolic root extract of the Polygonum hydropiper to demonstrate its estrogenic property (Goswami et al., 2008). This chromatographic fraction is responsible for alteration of expression of protein profile of both non pregnant and pregnant rats' uteri (Goswami et al., 2009). The plant Dysoxylum alliarium (Family: Meliaceae) is a medicinal plants mainly distributed in parts of Assam, Arunachal Pradesh, Meghalaya and in Sikkim of north east India. The bark of this plant is traditionally used by the ethnic tribal people of Arunachal Pradesh for the purpose of population control of domestic animals such as pigs and dogs. Laboratory screening of the bark extract of *D. alliarium* showed the loss of embryo during early gestation period in rats (Das et al., 2013). Isolation and identification of such compound with antifertility activity may be a valuable contribution in the field of contraceptive research. The information mentioned above showed that a large number of plants across the world contain potential compound for fertility control. In recent years, the scientists focused on the isolation of plant derived compound having antifertility property.

Phytoestrogen and its importance in reproductive health

The ovarian hormones estrogen and progesterone control the functions of uterus to achieve successful pregnancy. The estrogen and progesterone binds to their respective receptors to carry out the cellular functions. Any exogenous substances capable of altering the biological function of reproductive tissues must possess some chemical compounds with ability to modulate the function of estrogen and progesterone. These chemical substances may be structurally and functionally similar to that of the ovarian steroids. Plants are the natural resources of such compound having potentiality to use as reproductive function modulator in human and animals. These chemical substances bind to the hormone receptors and may mimic the function of ovarian hormones either in agonistic and antagonistic manner. Such type of compounds very often termed as phytoestrogen, plays a crucial role in manipulating the reproductive function of the uterus and ovaries. The phytoestrogens are the naturally occurring chemicals with estrogen like biological activity found in plants (Murkis et al., 1998). Thus, the phytoestrogens occupy an important place in the pharmaceutical research to develop new drug for manipulation of the function of reproductive organs. The manipulation of reproductive function is required when there is physiological condition of deficiency of the hormones or hormonal imbalance in the reproductive tissues and/or in the need of fertility control. In search of such compounds the plants are being tested and the chemical characterization of the plant derived compounds has been done in different laboratories of the world. Selection of such plants is based on the ethnobotanical information that provides the basic information on the use of such plant against a particular ailment.

Phytoestrogens are a family of non-steroidal chemically diversified plant-derived compounds having the effect on mammalin tissues similar to that of the ovarian estrogen (Murkies *et al.*, 1998). They may mimic or/and interact to the estrogen hormones in mammalian tissues. This group of compounds are categorised on the basis of their structural resemblance with estrdiol-17 β . Isoflavones, coumestans, Lignans, are the major phytoestrogens while there are many other phytoestrogens with structural diversity having estrogenic activity (Ososki and Kennelly, 2003). Estrogenic effect of herbs in reproductive system was first reported with adverse effects on mammalian development and fertility from

observations of animals consuming phytoestrogen-rich plants. Ewes grazing on estrogenic pasture rich in subterranean clover developed breeding problems in western Australia (Bennetts et al., 1946). The traditional herbal medicines used for controlling reproduction have adverse estrogenic effects on target organs and application of such herbal medicines to desired women terminate pregnancy and may cause abortion. Estrogenic effects of such herbal medicines have been widely investigated to formulate new product with safety and efficacy to control reproduction and other feminine reproductive ailments like menopausal symptoms, menstrual disorder etc. Screening of such herbal medicines involves the observation of effect of such medicines on vaginal epithelial cyclicity, endometrial receptivity, implantation, follicular development etc. Very often these phytoestrogens exert their effects on vagina, uterus by acting as an endocrine disruptor. They exert estrogenic effect by binding to the estrogen receptor with varied affinity (Forth and Cline, 1998; Branham, 2002). Most phytoestrogens bind to the estrogen receptors with lower affinity than estradiol-17â (Kuiper et al., 1997) and are weekly estrogenic. The genistein, daidzein, coumestrol are weak estrogen as compared to Estradiol-17â (Hopert et al., 1998). These weak estrogens act as estrogen agonist and mimic ovarian estrogen inducing cellular proliferation, maturation, cornification in estrogen responsive tissues. An indigenous herb of Thailand 'Pueraria mirifica' contains phytoestrogen 'deoxymiroestrol' and isoflavones such as daidzin, and genistein (Chansakaow et al., 2000). Such isoflavones were also isolated from the red clover 'Trifolium pratense' (Beck et al., 2004). Extract of Red clover Trifolium pratense increases the uterine weight dose-dependently and induce vaginal cornification showing estrogenic effect in Spraguedawley rats (Burdette et al., 2002). The effect of Pueraria mirifica was postulated to estrogenic on reproductive system in both sexes of rats (Malaivijitnond, 2004). The ethanol extract of Hibiscus rosa sinensis showed estrogenicity in immature albino rats (Vasudeva and Sharma, 2006). Orally administered soy extract proliferates the uterus of ovariectomised rats (Mosquette et al., 2006) and soy rich diet shows higher maturation value of vaginal epithelial cells revealing the estrogenicity of the soy food

(Chiechi et al., 2003). 'Resveratrol' a phytoestrogen available in the grape, induce vaginal epithelial cell maturation in ovariectomized rat (Hascalik et al., 2005). An estrogenic compound isolated from the plant 'Humulus lupulus' induced proliferation of vaginal and uterine mass of epithelial tissues (Milligan et al., 2002) and the compound has been identified as 8-prenylnaringenin (Milligan et al., 1999). The phytoestrogens may have antiestrogenic effect, they may block or alter estrogen receptors binding affinity acting as estrogen antagonist (Ososki and Kennelly, 2003). The balance between the estrogenicity and the antiestrogenicity is dependent on the hormonal milieu. For example, coumestrol rich diet induces onset of estrous cycle prepubertally in immature female, whereas same dose of diet inhibits ovarian cycle in adult female rats (Whitten et al., 1995). These phytoestrogens with different binding affinity to the estrogen receptors (ER) compete with the ovarian estrogen (E2) and alters the normal functions of reproductive tissues such as ovarian follicles, uterine and vaginal epithelial tissues and may explain the fertility regulatory activity in mammals. The mechanism of action of phytoestrogen involves more than one aspect of molecular response. The phytoestrogen may elicit genomic estrogenic response by binding to the estrogen receptor (ER) (Wang et al., 1996; Wang and kurzar, 1998). It may modulate epigenetic estrogenic response by influencing protein kinase A action and intracellular calcium (Ca2+) mobilization (Morley et al., 1992; Katzenellenbogen, 1996). There are many evidences that phytoestrogens may disrupt the endocrine system and may act as endocrine disruptor both in animals and humans (McLachlan, 2006). Administration of 1000 mg of suspension of tuberous root powder of the Pueraria mirifica increased the levels of both FSH and LH after 1 weak of treatment in OVX female wistar rats (Malaivijitnond, et al., 2004). The 'coumestrol' has profound effect to inhibit Gn-RH-induced LH release in vivo and reveals a concomitant hypothalamic site of action (McGarvey et al., 2001). Dietary genistein exerts estrogenic effect involving hypothalamic-pituitary axis in rats (Santell et al., 1996) and can modulate the prostaglandin production (Woclawek-Potocka et al, 2005). The phytoestrogens have been proposed to have potentiality for prevention and treatment of vascular

disease (Marsh, 2000) and to cure menopausal symptoms (Usui, 2006). The researches on the estrogenic compounds and their biological effects on animal and human are still required to evaluate the beneficial effect of the phytoestrogens.

Conclusion

Reproductive health of women is one of the prime factor for better health of the child or we can say it is the backbone of a healthy human society. However, disorders related to the women reproductive health is still a big enigma and challenging tasks in front of the modern health care system globally. The discovery of modern synthetic drugs for the regulation of reproductive health has able to mitigate this menace but with a couple of significant side effects. Therefore, scientists are inclines towards the traditional healthcare practices in quest of indigenous information of herbal origin traditionally used by the indigenous women for maintenance of their reproductive health issues. Nature has given plenty of medicines in the form of plant species which are used by the indigenous people since time immemorial. The phytocompounds present in these plants has potent capacity to treat various ailments including reproductive disorders especially in women. Realising the importance, the scientific community including WHO formulating various programmes for the documenting and screening of medicinal plants used for reproduction regulation. Proper exploitation of this traditional information will leads to the development of new drugs of herbal origin with lesser or no side effects for the beneficial of mankind especially female reproductive health.

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References

Almeida ER, Oliveira JRG, Lucena FRS, Silva CVNS, Soares RPF, Cavalcanti JB, Couto GBL. 2007. Embryofetotoxic effect and offspring postnatal development exposed to hydroalcoholic fraction extract of *Cissus sicyoides* L. during wistar rats pregnancy. J Med Plant Res. 1(5): 109-112.

Asongalem EA, Nana P, Foyet HS, Dimo T, Kamtchouing P. 2008. Antifertility and fetotoxic activities of *Acanthus montanus* aqueous extract in Wistar rats. Methods Find Exp Clin Pharmacol. 30(7): 521-528.

Beck V, Rohr U, Jungbauer A. 2005. Phytoestrogens derived from red clover: An alternative to estrogen replacement therapy? J Steroid Biochem Mol Biol. 94: 499-518.

Belachew D. 1994. Ethiopian traditional herbal drugs Part-III: Antifertility activity of 70 medicinal plants. J Ethnopharm. 44(3): 199-209.

Bennetts HW, Underwood EJ, Shier FL. 1946. A specific breeding problem of sheep on subterranean clover pasture in Western Australia. Aust Vet J. 22: 2-12.

Bhakuni DS, Goel AK, Jain S, Mehrotra BN, Srimal RC. 1990. Screening of Indian plants for biological activity Part-XIV. Indian J Exp Biol. 28: 619-637.

Branham WS, Dial SL, Moland CL, Hass BS, Blair RM, Fang H, Shi L, Tong W, Perkins RG and Sheehan DM. 2002. Phytoestrogens and micoestrogens bind to the rat uterine estrogen receptor. J Nutr. 132: 658-654.

Burdette JE, Liu J, Lantvit D, Lim E, Booth N, Bhat KPL, Hedayat S, Breemen RBV, Constantinou AI, Pezzuto JM, Farnsworth NR and Bolton JL. 2002. *Trifolium pratense* (Red Clover) exhibits estrogenic effects in vivo in ovariectomized sprague-dawley rats. J Nutr. 132: 27-30.

Chansakaow S, Ishikawa T, Sekine K, Okada M, Higuchi Y, Kudo M, et al. 2000. Isoflavones from *Pueraria mirifica* and their estrogenic activity. Planta med. 66: 572-575.

Chattopadhyay I, Biswas K, Bandopadhyay U, Banerjee RK. 2004. Turmeric and curcumin: Biological actions and medicinal applications. Cur Sci. 87(1): 44-53.

Chiechi LM, Putignano G, Guerra V, Schiavelli MP, Cisternino AM, Carriero C. 2003. The effect of a soy rich diet on the vaginal epithelium in post menopause: a rendomized double blind trial. Maturitus. 45: 241-246.

Chopra RN, Naayar SL and Chopra LC. 1956. Glossary of Indian medicinal plants CSIR, New Delhi.

Davis SR. 2001. Phytoestrogen therapy for menopausal symptoms? BMJ. 323: 354-355.

Dhawan BN, Patnaik GK, Rastogi RP, Singh KK and Tandon JS. 1977. Screening of Indian plants for biological activity, part VI. Indian j Exp Biol. 15:208-219.

Doi SAR, Al-Zaid M, Towers PA. 2005. Scott CJ and Al-Shoumer AS rregular cycles and steroid hormones in polycystic ovary syndrome. Hum Reprod. 20(9): 2402-2408

Fabricant DS and Farnsworth NR. 2001. The Value of

Fabricant DS and Farnsworth NR. 2001. The Value of Plants Used in Traditional Medicine for Drug Discovery. Environmental Health Perspectives. 109: 69-75.

Fillipov A. 1994. Medicinal plants of pelago of central chaco. J Ethnopharmacol. 44: 141-193.

Forth D and Cline JM. 1998. Effects of mammalian and plant estrogens on mammary glands and uteri of macaques. Am J Clin Nutr. 68: 1413s-1417s.

Garg SK, Mathur VS, Chaudhury RR. 1978. Screening of Indian plants for fertility activity. Indian J Exp Biol. 16: 1077-1079

Gebri E, Makonnen E, Zerihun L, Debella A. 2005. The possible mechanisms for the antifertility action of methanolic root extract of *Rumex steudelii*. African Health Science. 5(2): 119-125.

Glazier MG and Bowman MA. 2001. A review of the evidence for use of phytoestrogens as a replacement for traditional estrogen replacement therapy. Arch Intern Med. 161: 1161-1172.

Goswami P, Hazarika A, Sarma H. 2008. Thin layer chromatographic fraction of root extract of *Polygonum hydropiper* induces vaginal epithelial cell maturation in adult ovariectomized albino rat. J endocrinol Reprod. 12(1): 39-46. Goswami P, Hazarika A, Sarma H. 2009. Root extract of *Polygonum hydropiper* alters the expression of rat uterine protein profile in the presence and absence of ovary *in-situ* during periimplantation period: an evidence on SDS-PAGE. J Reprod Contracep. 20(4): 223-236.

Griffin PD. 1988. Plants for fertility regulation. In: Research in Human reproduction, Biennial report (1986-1987). Diczfalusy, E.; Giffin, P.D. and Khanna, J. (eds) WHO. Geneva Pp: 229-239.

Guyton AC and Hall JE. 2006. Text Book of Medical Physiology, eleventh edition, Philadelphia. Sounders.

Hascalik S, Celik O, Tamser M, Mizrak B. 2005. Effects of resveratrol, raloxifen, tibolone, and conjugated equine estrogen on vaginal squamous cell maturation of Ovariectomized rats. Gynecol Obstet Invest. 60: 186-191.

Hazarika A, Sarma H N 2006. *Polygonum hydropiper* crude root extract mimics estrogenic properties in females: Evidence of uterine protein profiles studied by sodium dodecyl sulfate polyacrylamide gel electrophoresis. Reprod Med Biol. 5:155-160.

Hoffman GE and Zup SL. 2003. Good Versus Evil: Changing the Approach to Hormone Replacement Therapy. Endocrinol. 144: 4698-4699.

Holst L, Wright D, Haavik S, Nordeng H. 2009. The use and the user of herbal remedies during pregnancy. J Alt Complement Med. 15(7): 787-792.

Hopert A-C, Beyer A, Frank K, Strunk E, Wunsche W, Vollmer G. 1998. characterization of estrogenicity of phytoestrogens in an endometrial-derived experimental model. Environ Health Persp. 106(9): 581-586.

Islam MN, Sulaiman SA, Kapitonova MY, Sahil SM. 2007. Effects of an indigenous herbal formulation on gonadotrophs of the pituitary gland of the rat. Malaysian J Med Sci. 14(1): 23-27.

Jain A, Katewa SS, Chaodhary BL, Galav P. 2004. Folk herbal medicines used in birth control and sexual diseases by tribals of southern Rajasthan. J Ethnopharm. 90(1): 171-177.

Joseph J and Collins ND. 2005. Phytotherapeutic management of endocrine dysfunctions. *Nutri News.* Douglas Laboratories. www.douglaslabs.com.

Kala CP, Dhyani PP and Sajwan BS. 2006. Developing the medicinal plants sector in northeastern India: challenges and opportunities. J Ethnobio Ethnomed. 2: 32.

Katzenellenbogen BS, Choi I, Delage-Mourroux R, Ediger TR, Martini PG, Montano M, Sun J, Weis K, Katzenellenbogen JA. 2000. Molecular mechanisms of estrogen action: selective ligands and receptor pharmacology. J Steroid Biochem Mol Biol. 75(5): 279-85.

Keshri G, Kumar S, Kulshreshthra DK, Rajendran SM, Singh MM. 2008. Post coital interceptive activity of *Wrightia tinctoria* in Sprague-dawley rat: a preliminary study. *Contraception*. 78: 266-270.

Keshri G, Lakshmi V, Singh MM. 2003. Pregnancy interceptive activity of *Melia azedarach* Linn. in adult female Sprague-Dawley rats Contraception. 68(4): 303-306.

Keshri G, Oberoi RM, Lakshmi V. 2007. Contraceptive and hormonal properties of stem bark of *Dysoxylum binectariferum* in rat and docking analysis of rohitokine, the alkaloid isolated from active chloroform soluble fraction. Contracep. 76: 400-407.

Kirtikar KR and Basu BD. 1998. Indian medicinal plants, Vol-III, 2nd ed. New Delhi, Periodical expert book agency.

Kokoska L and Janovska D. 2009. Chemistry and pharmacology of *Rhaponticum carthamoides*: A review. Phytochem. 70: 842-855.

Kuiper GGJM, Carrisson B, Grandien K, Enmark E, Haggblad J, Nilsson S, Gustafsson JA. 1997. Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors - α and β . Endocrin. 138: 863-870.

Lans C. 2007. Ethnomedicines used in Trinidad and Tobago for reproductive problems. J Ethnobiol Ethnomed. 3:13.

Lee KH. 2000. Research and future trends in the pharmaceutical development of medicinal herbs from Chinese medicine. Public Health Nutrition. 3(4A): 515-522.

Malaivijitnond S, Kiatthipipat P, Chershewasart W, Watanabe G, Taya K. 2004. Different effects of *Pueraria mirifica*, a herb containing phytoestrogens, on LH and FSH secretion in gonadectomized female and male rats. J Pharmacol Sci. 96: 428-435.

Marsh JD. 2000. Phytoestrogens and vascular therapy. J Am Coll Cardiol. 35: 1986-1987.

McGarvey C, Cates PS, Brooks AN, Swanson IA, Milligan SR, Coen CW, O'byrne KT. 2001. Phytoestrogens and gonadotropin-releasing hormone pulse generator activity and pituitary luteinizing hormone release in the rat. Endocrinol. 142(3): 1202-1208.

McLachlan JA. 2006. Endocrine disrupters and female reproductive health. J Clinical Endocrinol Metabol. 20(1): 63-75.

Miligan SR, Kalita JC,, Heyerick A, Rong H, De Cooman L, and De Keukeleire D. 1999. Identification of a potent phytoestrogen in hops (*Humulus lupulus* L.) and beer. J Clinical Endocrinol Metabol. 83(6): 2249-2252.

Milligan S, Kalita J, Pocock V, Heyerick A, De Cooman L, Rong H and De Keukeleire D. 2002. Oestrogenic activity of the hop phyto-estrogen, 8-prenylnaringenin. Reproduct. 123: 235-242.

Miyazawa M and Tamura N. 2007. Inhibitory compound of tyrosinase activity from the sprout of *Polygonum hydropiper* L. (Benitade). Biol Pharm Bull. 30(3): 595-597.

Morley P, Whitfield JF, Vanderhygen BC, Tsang BK, Schwarz JL. 1992. A new, non-genomic estrogen action: the rapid release of intracellular calcium. Endocrinol. 1311: 1305-1312. Mosquette R, Simoes M de J, Silva IDCG da, Oshima CTF, Oliviera-Filho RM, Haidar MA, Simoes RS, Baracat EC and Soares Junior JM. 2007. The effects of soy extract on the uterus of castrated adult rats. *Maturitus*. 56: 173-183.

Murkies AL, Wilcox G and Davis SR. 1998. Phytoestrogens. J Clin Endocrinol Metabol. 83; 297-303.

Murugan V, Shareef H, Sarma GVSR, Ramanathan M, Suresh B. 2000. Antifertility activity of *Alangium salviifolium*. Ind J Pharmacol. 32: 388-389.

Nath D, Sethi N, Singh RK and Jain AK. 1992. Commonly used Indian abprtificient plants with special reference to their teratological effects in rat. J Ethnopharm. 36: 147-154.

Nwafor PA and Okwuasaba FK. 2001. Contraceptive and estrogenic effect of a methanol extract of *Cassis nigricans* leaves in experimental animals. Pharmaceut Biol. 39(6): 424-428.

Nyinawumuntu A, Awe EO, Ojewole JAO. 2008. Uterolytic effect of *Hypoxis hemerocallidea* Fisch. & C. A. Mey. (Hypoxidaceae) corm ['African Poteto'] aqueous extract. J Smooth Muscle Res. 44(5): 167-176.

Oluyemi KA, Okwuonu UC, Baxter DG, Oyesola TO. 2007. Toxic effects of methanolic extract of *Aspilia africana* leaf on the estrous cycle and uterine tissues of winstar rats. Int J Morphol. 25(3): 609-614.

Ososki AL, and Kennelly EJ. 2003. Phytoestrogens: a review of the present state of research. Phytotherap Res. 17: 845-869.

Philipson JD, Anderson LA. 1988. Ethnopharmacology and western medicine. J Ethnopharmacol. 25: 61-72.

Prakash AO and Mathur R. 1979. Biochemical changes in the rat uterine tissue following *Embelia ribs* burm extract. Ind J Pharmac. 11(2): 127-134.

Premkumara GAS, Ratnasooriya WD, Tillekeratne LMV. 1995. Studied on the post coital contracptive mechanism of the crude extract of Sri Lankan marine red algae. Contracep. 52: 203-207.

Ratnasooriya WD, Premkumara GAS, Tillekeratne LMV. 1994. Postcoital contraceptive activity of crude extracts of Sri Lankan marine algae. Contracep. 50: 291-299.

Reddy CS, Reddy KN, Rao T and Pattanaik C. 2007. Ethnobotanical studies on medicinal plants used by the Chenchus of Nallamalais in Kurnool district, Andhra Pradesh, India. Res J Med Plant. 1(4): 128-133.

Rithaporn T, Monga M and Rajesekharan M. 2003. Curcumin: A potential vaginal contraceptive. Contracep. 68: 219-223.

Sadik Md G, Gafur MA, Bhuiyan MSA, Rahman MM, Biswas HU. 2001. Antifertility action of the alkaloidal fraction of *Pergularia daemia*. The Sciences. 1(4): 217-219.

Santell RC, Chang YC, Nair MG, Helferich WG. 1997. Dietary genistein exerts estrogenic effects upon uterus, mammary gland and the hypothalamic/pituitary axis in rats. J Nutr. 127: 263-269.

Sarma HN and Mahanta HC. 2000. Effects of composite root extract on histological structure of graffian follicles and endometrial epithelium in albino rat. Contracep. 61(5): 335-339. Shibeshi W, Makonnen E, Zerihun L, Debella A. 2006. Effect of Achyrenthes aspera L. On fetal abortion.

2006. Effect of *Achyrenthes aspera* L. On fetal abortion, uterine and pituitary weight, serum lipids and hormones. African Health Sci. 6(2): 108-112.

Srivastava SR, Keshri G, Bhargavan B, Singh C, Singh MM. 2007. Pregnancy interceptive activity of the roots of Calotropis gigantea Linn. in rats. Contracep. 75(4): 318-322.

Upadhyay SN, Kaushic C and Talwar GP. 1990. Antifertility effects of neem (*Azadireccta indica*) oil by single intrauterine administration: a novel method for contraception.

Proceedings: Biol Sci. 242(1305): 175-179.

Usui T. 2006. Pharmaceutical prospects of phytoestrogens. Endocrine Journal. 53(1): 7-20.

Vasudeva N and Sharma SK. 2007. Post coital antifertility activity of hibiscus rosa sinensis Linn. roots. *eCam.* 1-4.

Vikers KA, Jolly KB, Greenfield SM. 2006. Herbal medicine: women's views, knowledge and interaction with doctors: a qualitative study. BMC Complement Alternat Med. 6: 40.

Wang C and Kurzer MS. 1998. Effects of phytoestrogen on DNA synthesis in MCF-7 cells in the presence of estraaddiol or growth factors. Nutr Cancer. 3: 90-100.

Wang C, Sathyamoorthy N, Phang JM. 1996. Molecular effects of genistein on receptor mediated pathways Carcinogenesis. 17: 271-275.

Wanibichi H, Kang JS, Salim EI Morimora K and Fukushima S. 2003 Toxicity vs beneficial effects of phytoestrogens. Pure Appl. Chem. 75(11-12): 2047-2053.

Whitten PL, Liwis C, Russell E, Naftolin F. 1995. Potential adverse effects of phytoestrogens. J Nitr. 125: 771-776 Williamson L M, Parkes A, Wight D, Petticrew M and Hart G J. 2009. Limit to modern contraceptive use among young women in developing countries: A systematic review of qualitative research. Reprod Health. 6:3.

Woclawek-Potoka I, Acosta TJ, Korzekwa A, Bah MM, Shibaya M, Okuda K, Skarzynski DJ. 2005. Phytoestrogens modulate prostaglandin production in bovine endometrium: Cell type specificity and intracellular mechanisms. Exp Biol Med. 230: 326-333.

World Health Organisation. 2004. Reproductive health strategy to accelerate progress towards the attainment of international development goals and targets. Geneva, World health Organisation.

Yadav R and Jain GC. 1999. Antifertility effect of aquous extract of seeds of *Cassia fistula* in female rat. Adv Contracep. 15: 292-301.