Effect of Medicinal Plant on Male Reproductive System: A Review

Alka Singh and UVS Teotia*

Deparment of life Sciences, Sri Venketheshwara University, Gajraula, U.P

Abstract

The aim of this review was to provide a comprehensive summary of medicinal plants used as antifertility agents in males throughout the world by various tribes and ethnic groups. We undertook an extensive bibliographic review by analyzing classical text books and peer reviewed papers, and further consulting well accepted worldwide scientific databases. Plants, including their parts and extracts, that have traditionally been used to facilitate antifertility have been considered as antifertility agents. In this paper, various medicinal plants have been reviewed for thorough studies such as *Catharanthus roseus*, *Solanum xanthocarpum* and *Momordica charantia*. Many of these medicinal plants appear to act through an antizygotic mechanism. This review clearly demonstrates that it is time to expand upon experimental studies to source new potential chemical constituents from medicinal plants; plant extracts and their active constituents should be further investigated for their mechanisms. This review creates a solid foundation upon which to further study the efficacy of plants that are both currently used by male as traditional antifertility medicines, but also could be efficacious as an antifertility agent with additional research and study.

Keywords: antifertility agent efficacy, literature review, medicinal plants

*Corresponding Author:

Email: uvsteotia2017@gmail.com

Phone No:0999739999

Introduction

Antifertility agents are drugs that control fertility [1]. In males, it prevents spermatogenesis, inhibits testosterone, or affects the gonadotrophin of the organs or the mortality of sperm. Currently, population size is being controlled in many developing countries [2]. Oxyphenbutazone, indomethacin, and acetyl salicylic acid inhibit prostaglandin formation and manifest antifertility activities in albino male and female rabbits. The reproductive process is affected by indomethacin and oxyphenbutazone in male rabbits. It has also been observed that many plants may have spermicidal activity. Medicinal plants are a great gift of nature as a cure-all for a plethora of human problems [3]. Various institutes in South Asia have long-established traditions of cultivating the faculties of the younger generation in the emerging field of science and technology. Currently, many scientists in that region have an ongoing mandate to educate and train the younger generation to facilitate future innovation and advancement in the field, while also working with venture capital elements and the corporate sector at the same time to optimize their research opportunities [4]. It goes without saying that modern scientific investigation has proven the medicinal value of medicinal plants. Herbal medicines and their derivatives have been incorporated into traditional medicine virtually since the beginning of recorded history. But it is only in recent times that the broader use of medicinal plants is beginning to garner acceptance in the more expansive international domain. There are certain bottlenecks in the process, including but not limited to the lack of quality control and toxicological studies, the imperative to increase product shelf life, and compliance with international regulatory standards that need to be overcome before their full market potential can be realized. The Ayurvedic and Unani system of medicine is an indigenous treatment, very prevalent in South Asia and popular among large populations in India, Pakistan, Bangladesh, and Sri Lanka. More specifically, Ayurvedic medicine is part of the South Asian culture where it is practiced among a large segment of the population [5]. Due to its regional popularity, Ayurvedic medicine has achieved an exponential growth over the past 5 decades in South Asia. On a practical basis, Unani medicine is innovative in that its practitioners have accepted and managed to avoid many of the challenges that practicing professionals make, including issues with practice–patient relations, forms of intervention, and disease conceptualization itself. This knowledge that is presently used to control conception, though still in use among tribal populations, requires further scientific examination, so that the active components present in

such plants which are capable of obstructing the reproductive cycle can be properly delineated and utilized.

Herbal medicine today

It is estimated that about 4 billion people (80%) of the world population rely primarily on herbal medicine for their health care needs [6]. It is in this light that WHO encourages the use of herbal preparations for the treatment of some local health problems particularly in developing countries where they are readily available, easily affordable and already integrated into the people's cultures.

Balandrin et al reported that at least 25% of active compounds in synthetic drugs currently prescribed were first identified in plant sources [7]. Several plants contain active principles that have been proved beneficial through extensive laboratory tests and repeated clinical trials. For example, salicylic acid, a precursor of aspirin was originally derived from Salix carolina (willow tree); opium, morphine and codeine from Papaver somniferum (poppy plant); reserpine (an antihypertensive) from Rauwolfia vomitoria; artesiminin from Artemisia annua; digoxin from Digitalis purpurea; quinine (antimalaria) from the bark of Cinchona plant; vincristine and vinblastine (antitumor agents) from Catharanthus roseus (foxglove plant) [8]. Herbs and herbal products have proved to be effective and safe alternatives to costly and toxic factory made drugs. Hence there is a renewed interest in the use of herbal preparations [9]. Besides promotion of health, other reasons for the current popular use of herbal products or remedies are dissatisfaction or lack of efficacy of conventional drugs, limited treatment options for serious illness, belief that naturals are safer or better, cultural or spiritual preference, toxicity or serious side effects associated with modern drugs [10,11]. Plant extracts are now processed as snips, sauces, tablets, tinctures, encapsulated powders, oral sprays and lozenges. Herbal tonics and potions are taken regularly as prevention against diseases or rejuvenation following recovery

from illness or injury. There is an increasing demand for plant based industrial products, pharmaceuticals, nutriceuticals, phytomedicines and herbal tea. Although traditional, complementary and alternative medicines are popular in developing countries and in developed world there is an increasing shift from synthetic to natural, WHO however stresses on scientific validation or verification, based on safety, efficacy and quality of this form of therapy [12]. The herbal recipes are prepared from one or a combination of two or more plants and in most cases administered over a prolonged period of time. It is common practice in Nigeria that herbal products are administered over prolonged period and by persons that have little or no knowledge of science [13]. The constituents of these recipes elicit varied physiological activities. There has been concern over adverse effects on reproduction or systemic toxicity due to prolonged use of medicinal products [14]. Since 1978 when WHO identified over 20,000 species of medicinal plants which are widespread in tropical countries, several other plants are yet to be validated scientifically for the acclaimed efficacy and especially their effects on reproductive organs and functions.

Physiology of male reproduction

The male genital tract consists of the testicles and epididymides as well as accessory sex glands (prostate, seminal vesicles) and vas deferens that lead to the penile urethra. The structure of the mammalian testis (a paired organ) reflects its functions of spermatogenesis which occur within the seminiferous tubules and androgen (testosterone) secretion by the Leydig cells [15]. Spermatogenesis is exocrine, whereas testosterone secretion by Leydig cells is endocrine. Male reproduction is regulated by release of follicle stimulating hormone (FSH) and luteinising hormone (LH) from the anterior pituitary [16,17]. The adenohypophyseal hormones are in turn regulated by the release of gonadotropin-releasing hormone from the hypothalamus. The levels

of LH and FSH are controlled by negative feedback mechanisms which appear to be independently controlled [18]. Whilst LH stimulates the Leydig cells to secrete testosterone, FSH and testosterone maintain spermatogenesis. Testosterone is the primary androgen and controls the functional activity of all male reproductive tract structures. The roles of testosterone in spermatogenesis, sperm maturation in epididymis, sex drive (libido), secondary sex characteristics and in promoting the growth, development and functions of the epididymis and other accessory organs are well documented [19]. In mammals, the unique location of the testis in the scrotum provides an optimum environment for spermatozoa production. After spermiation, the spermatozoa move through the seminiferous tubules and collect in the rete testis from where they migrate via ductuli efferentia to the epididymis. Several physiological studies have described the existence of blood - testis or blood - epididymis barrier and demonstrated that substances of high molecular weights do not readily permeate the testis and epididymis. These authors postulated that various carrier mechanisms are utilized as means of transporting substances across their epithelia to provide favourable microenvironment for the developing spermatozoa. As the developing spermatozoa do not receive nutrients from the capillaries, the gametes are nourished by the Sertoli cells [20]. Testicular spermatozoa are immotile and incapable of progressive movement, but acquire this characteristic during transit in the caput and corpus epididymis [21]. The epididymis has both secretory and resorptive functions. The epididymis of mammals is responsible for the transport, concentration, maturation and storage of spermatozoa. Epididymal transport requires several days to weeks depending on the species and takes about 8 days in the rat, but can be faster in sexually active males [22]. Epididymal parameters are widely used and provide a simple but sensitive method of assessing effects of substances on male reproduction especially at the testicular or epididymal site of action. Sperm

motility, sperm count, viability and morphology of sperm cells are end points used for evaluation of fertilizing potentials of animals. Sperm count is highly correlated with fertility and considered one of the most sensitive tests since it gives the cumulative result of all stages in spermatogenesis There is currently no satisfactory method for assessing semen samples in rats during life. Terminal sampling from cauda epididymis is considered a preferred site in rat as it has optimum conditions. Sperm motility, sperm count, viability and morphology of sperm cells are evaluative parameters and have been used to identify several plants with antispermatogenic and or anti-androgenic activities [23].

Effects of medicinal plants on reproductive functions

In several countries and all through the ages, medicinal plants have been widely used to enhance or regulate fertility. In Nigeria, the folkloric uses of plant preparations for reproduction related purposes are well known and documented [24]. Elsewhere, Gupta et al reported that herbal contraceptives are used because of affordability, ease of availability from local sources and less side effects. In folkloric medicine of many developing countries, large numbers of plants are used as abortifacient, contraceptive or sterility agents. Laboratory rodents are frequently used as animal models to study effects of medicinal plants on reproduction. Of the animal models, rats are often used to study a wide range of normal functions and pathophysiological conditions [25]. It is established that gossypol, a cotton plant extract inhibits spermatogenesis and sperm motility [26]. The effect of gossypol on spermatogenesis was discovered when a group of rural Chinese males who consumed raw homemade cotton seed oil became infertile. In a study, Chandiran et al observed a reduction in sperm motility, sperm concentration and abnormal morphology following the administration of ethanolic extract of Caesalpinia digyna root for 55 days. These researchers also demonstrated evidence of recovery in the animals after withdrawal of treatment

between 55th to 110th days. A restoration of sperm quality to normal levels after withdrawal of administration of 50% ethanolic extract of Aegle marmelos was reported by Chauhan et al. Similar harmful effects of methanolic extract of Ricinus communis and methanolic pod extract of Albizzia lebbeck resulting in low sperm count, reduced motility, viability and abnormal morphology were reported. Extracts of plants may affect androgen synthesis either by inhibiting Leydig cell function or disrupting the hypothalamic - pituitary axis. Raji et al attributed the adverse effect of Ricinus communis to gonadal disruption in testosterone secretion.

An accumulation of evidence suggest that the reduced weights of testes, epididymis, seminal vesicles and prostate glands of experimental animals following oral administration of Albizia lebbeck bark [27] were as a result of low serum or plasma testosterone. Other studies revealed disruption or hypoplasia of seminiferous tubules, erosion of germinal epithelium and disorganized histoarchitecture of the testes [28] and disarray of sperm population dynamics. There are also reports indicating that body and reproductive organ weights, sperm counts, viability, motility and morphology were increased by extracts of Phoenix dactylifera [29]. Other studies have confirmed the profertility effects of several plants as reflected by increases in weights of testes and accessory sex organs, sperm motility, sperm count and viability [30]. Increased level of testosterone was reported to be responsible for the enhanced testicular functions following oral administration of frankincense (Boswellia thurifera) [31]. In Jordanian folkloric medicine, frankincense is used as an aphrodisiac and in promoting fertility. Enhanced testicular function and stimulation of male sexual maturation have been demonstrated following oral administration of aqueous extract of Massularia acuminate [32]. Massularia acuminata stem is commonly used as chewing stick in southern Nigeria and claimed to have aphrodisiac property also reported that spermatogenesis was enhanced as reflected by increases in sperm count, sperm

motility, viability of spermatozoa and increases in testosterone level when rats were fed ginger (Zingiber officinale) for 30 days.

Since the discovery of phytoestrogens and steroidal substances, there have been growing research interests in crude plant extracts or products of plant origin as sources of antifertility agents. In India and China with heavy population burden, there are ongoing efforts to develop natural contraceptives of plant origin that are less toxic, cheap, readily available, self administrable and that have completely reversible effects [33]. Although sterilization, abortion and contraception are the main ways of birth control, contraception seems most popular and acceptable. A contraceptive prevents ovulation and or fertilization whereas an abortifacient acts after implantation has occurred. Interceptives prevent embryonic implantation after fertilization has taken place. The synthetic contraceptives which are in popular demand cannot be used for a long time because of their numerous side effects. Interestingly, many medicinal plants have been shown to possess antiovulatory, interceptive, contraceptive, ecbolic, emmenagogic, oxytocic and abortifacient properties [34]. Result revealed that the contraceptive effects of Asparagus pubescens root were exerted through mechanism that control preovulatory release of LH, prolactin and progesterone. Animal studies have shown that extracts of several plants reduced FSH, LH, progesterone and estradiol levels. For example, extracts of Garcinia kola seed [35], Cola nitida, Afrormosia laxiflora and Pterocarpus erinaceous were reported to have reduced the serum or plasma concentrations of these hormones. Similar observations were made by Kumar et al that a decrease in FSH delayed follicle maturation in the preovulatory phase and interfered with conception. It is evident from these reports that a reduction in FSH and LH impaired ovarian steroidogenesis and function. Several animal studies have revealed antizygotic, blastocytotoxic, antiimplantation and abortifacient properties of water and organic solvent

extracts of many commonly used medicinal plants, sometimes in dose dependent manner. In an investigation of antifertility property of a triterpenoid glycoside isolated from Dalbergia saxatilis in female rats, Scientist observed a decrease in maternal body weights, inhibition of conception and significant decreases in mean day 20 foetal crown-rump lengths. Similar observations on antifertility, antiimplantation or pregnancy interceptory properties suggestive of anovulatory, antiprogesterogenic or estrogenic effects have been made on extracts of Rivea hypocrateriformis, Myrisine guianensis, Morinda citrifolia and Spondias mombin. However, the strong abortifacient and antiimplantation properties of Achyranthes aspera validated by Vasudeva and Sharma was said not to be due to an imbalance of ovarian hormonal profile [36]. Sensitivity of experimental animals, dose of extract used, period and route of administration as well as physiological or pharmacological mechanisms are some of the factors affecting the implantation process.

In many cultures and throughout the ages, various parts of medicinal plants have been used to induce labour. The persistent use of several medicinal plants by traditional birth attendants and pregnant women in western Uganda to induce labor has recently been documented (Kamatenesi-. Smooth muscles of the uterus are sensitive to acetylcholine or prostaglandins and can be made to contract even by stretching. It is also known that spontaneous motility of the uterus is modulated by sex steroids [37]. The use of crude extracts or plant preparations as oxytocic indicates that some plants are actually potent. Mahomed and Ojewole [38] validated the uterotonic activity of an aqueous extract of Harpagophytum procumbens, a South African medicinal plant reputed for its traditional use as an obstetric remedy for induction of labour and expulsion of retained placenta. The mechanism of antiimplantation activity of Monecha ciliatum has been explained by its strong uterotonic property [39]. Similarly, Musanga cecropioides, a common Nigerian medicinal plant used for its oxytocic effect has been reported to increase uterine contraction in a

dose -dependent manner [40]. Oxytocin is normally an endogenous hormone that stimulates uterine contraction via stimulation of increased intracellular calcium ions, whereas acetylcholine is also an endogenous muscarinic receptor stimulator that produces uterine smooth muscle contraction via the activation of M2 and M3 receptors located within the myometrium [41]. However, other in vitro studies revealed relaxant effects of various substances on the smooth muscle of the uterus [42]. Hazarika and Sarma used vaginal smear to monitor the oestrous cycle of female albino rats given methanolic extract of Polygonum hydropiper at a dose of I g/kg body weight daily for three consecutive cycles and reported alteration of ovarian endocrine function. Irregularity of oestrous cycle may cause distortion of endometrial function which may in turn lead to a failure of implantation and pregnancy. Some other animal studies have revealed no -adverse effects of a few plant extracts on female reproductive functions. Costa-Silva et al reported that Carapa guianensis seed oil administered orally during the period of organogenesis failed to impair implantation and induce the death of foetuses. Similarly, Hypericum perforatum (St. John's wort), a medicinal plant used in the treatment of depression and psychiatric disorders was found to be neither toxic to mother rat nor cause interceptory activity during organogenesis [43]. Watcho et al have also demonstrated the favourable development, implantation and uterotrophic activities of Ficus asperifolia lending credence to the popular use of this plant for treating infertility or sterility in women in the Cameroons. Aqueous extract of Stevia rebaudiana at the test doses did not present any complication in pregnancy or teratogenicity. Similar studies have shown that most pure compounds of Azadirachta indica had low embryo- and foeto-toxicity compared with the unprocessed material. Estrogenic substances are also known to cause an increase in uterine wet weight, vaginal cell cornification and branching of mammary gland duct. Furthermore, estrogenic substances may expel ova from the oviduct, disrupt luteotrophic

activity of the blastocyst and cause imbalance in endogenous estrogen and progesterone. Thus, plants should be evaluated for their effects during gestation and lactation periods as they might produce adverse side effects in the dams and offspring [44].

Table 1: List of Plants Showing Antifertility Activity

Plant	**Type**	**Dose/body weight (mg/kg)**	**Activity**
Cichorium intybus	50% ethanolic extract	50	Anti-implantation
Cuscuta reflexa	Ethanolic extract	800	Anti-implantation
Rubia cordifolia	Ethanolic extract	250	Anti-implantation
Urtica diocia	Ethanolic extract	250	Anti-implantation
Abroma augusta	Petroleum ether	50	Anti-implantation
Curcuma longa	Petroleum ether	200	Anti-implantation
Plumbago rosea	Acetone extract	200	Anti-implantation
Aloe barbadensis	Aqueous extract	100	Anti-implantation
Abutilon indicum	50% aqueous methanolic extract	500	Anti-implantation
Artemisia vulgaris	Methanlic extract	300 and 600	Anti-implantation
Striga orobanchioides	Ethanolic extract	200	Anti-implantation
Acalypha indica Linn	Ethanolic extract	600	Estrogenic activity
Enicostemma axillare	Ethanolic extract	375 and 750	Antispermatogenic
*Mondia whitei*Linn	Ethanolic extract	400	Antispermatogenic
Moringa oleifera	90% ethanol extract	175	Abortifacient
*Curcuma longa*Linn	70% alcoholic extract	500	Antispermatogenic
*Abrus precatorius*Linn	70% methanolic extract	20 and 40	Antifertility
Aegle marmelos	50% ethanolic extract	100, 200, and 300	Antifertility effect
Albizzia lebbeck	Methanolic extract	50, 100, and 200	Antifertility effect
Bacopa monnieri	Dry powder	250	Antispermatogenic
Cannabis sativa	Alcoholic extract	20	Antispermatogenic
Dendrophthoe falcata	70% methanolic extract	100	Antispermatogenic
Fadogia agrestis	Aqueous extract	18, 50, and 100	Adverse effects on male rat testicular function
Juniperus phoenica	Ethanolic extract	Intraperitoneal injections of 400	Antifertility activity

Leptadenia hastata	Aqueous extract	100, 200, 400, and 800	Antispermatogenic activity
Ocimum sanctum	Benzene extract	300	Antifertility property
Quassia amara	Chloroform extracts	Single daily intramuscular injections of the extract for 15 d	Antifertility effect
Syzygium aromaticum	Hexane extract	15, 30, and 60	Degenerative changes in the seminiferous tubules
Terminalia bellirica	Alcoholic extracts	50 mg/d	Antifertility effect

References:

1. Narayana A. and Subhose V., "Standardization of Ayurvˇedic formulations: a scientific review," Bulletin of the Indian Institute of History of Medicine, vol. 35, no. 1, pp. 21–32, 2005.
2. Abdulazeez, M.A., Ameh, A.D., Ibrahim, S., Ayo, J.O. and Ambali, S.F., Effect offermented seed extract of Carica papaya on litters of female Wistar rats (Rattus norvegicus), African Journal of Biotechnology, 8(5): 854 – 857, 2009.
3. Abu, A.H., Ofukwu, R.A. and Mazawaje, D., A study of traditional animal health care in Nasarawa state, Nigeria. American- Eurasian Journal of Sustainable Agriculture 3(3): 468 -472, 2009.
4. Adamu, S., Fatihu, M.Y., Useh, N.M., Mamman, M., Sekoni, V.D. and Esievo, K.A.N., Sequential testicular and epididymal damage in zebu bulls experimentally infected with Trypanosoma vivax. Veterinary Parasitology 143(1):29-34, 2009.
5. Adedapo, A.A., Abatan, M.O. and Olorunsogo, O.O., Toxic effects of some plants in the genus Euphorbia on haematological and biochemical parameters of rats. Veterinarski Arhiv 74:53-62, 2004.

6. Adeeko, A.O. and Dada, O.A., Chloroquine reduces the fertilizing capacity of epididymal spermatozoa in rats. African Journal of Medicine and Medical Sciences 27: 63 – 68, 1998.
7. Balandrin, P.M. Klocke, J.A., Wurtele, E.S. and Bullinger, W.H., Natural plant chemicals: sources of industrial and medicinal materials. Science 228: 1154 – 1160, 1985.
8. Akaneme, F.I., Identification and preliminary phytochemical analysis of herbs that can arrest threatened miscarriage in Orba and Nsukka towns of Enugu state. African Journal of Biotechnology 7(1): 6 – 11, 2008.
9. H. Gavaghan, "Koop may set up new centre for alternative medicine," Nature, vol. 370, no. 6491, p. 591, 1994.
10. Atawodi, S.E, Ameh, D.A Ibrahim, S. Nok, A.J., Mamman, M. and Galadiman, M.J., In vitro trypanocidal effects of methanolic extracts of some Nigerian savannah plants .African Journal of Biotechnology 2(9):317 – 321, 2006.
11. Atawodi, S.E. and Alafiatayo, A.A., Assessment of phytochemical and antitrypanosomal properties of some extracts of leaves, stem and root bark of Landolphia owarensis P.Beauv. Journal of Ethnopharmacology 114: 207 – 211, 2007.
12. Azmeera M, Elumalai A, Eswaraiah MC and Mathangi N., An Updated Review on Anti-fertility Plants. 2 (1):4-6, 2012.
13. Balasinor, N., Bhan, A., Paradkar, N.S., Shaikh, A., Nandedkar, T.D., Bhutanik, K. and Roy- Chaudhaury, M., Postnatal development and reproductive performance of F1 progeny exposed in utero to an ayurvedic contraceptive: Pippaliyadi yoga. Journal of Ethnopharmacology 109: 406 – 411, 2007.

14. Barret, M.P. and Fairlamb, A.H., The biochemical basis of arsenical diamidine cross resistance in African trypanosomes. Parasitology Today 15: 136 – 140, 1999.
15. Amann, R. P. and V. K. Ganjam., Effects of hemicastration or hCG-treatment on steroids in testicular vein and jugular vein blood of stallions. J. Androl. 3:132, 1981.
16. Bolender, R. P., Sterology and its uses in cell biology. An. NY Acad. Sci. 383:1, 1982.
17. Courot, M. Endocrine control of the supporting and germ cells of the impuberal testis. J. Reprod. Fertil. 2:89, 1967.
18. N. Balasinor,A. Bhan, N. S. Paradkar et al., "Postnatal development and reproductive performance of F1 progeny exposed in uteroto an ayurvedic contraceptive: Pippaliyadi yoga," Journal of Ethnopharmacology, vol. 109, no. 3, pp. 406–411, 2007.
19. D. John, "One hundred useful raw drugs of the Kani tribes of Trivandrumforest division,Kerala, India," International Journal of Crude Drug Research, vol. 22, no. 1, pp. 17–39, 1984.
20. E. L. Cooper, "Ayurveda and eCAM: a closer connection," Evidence-Based Complementary and Alternative Medicine, vol. 5, no. 2, pp. 121–122, 2008.
21. K. Joshi, Y. Ghodke, and B. Patwardhan, "Traditional medicine to modern pharmacogenomics: Ayurveda Prakriti type and CYP2C19 gene polymorphism associated with the metabolic variability," Evidence-Based Complementary and Alternative Medicine, vol., Article ID 249528, 5 pages, 2011.
22. Kalita JC, Chakrabarty A, Tanti B. Assessment of Antifertility activity of some traditionally used plants by different ethnic communities in three districts of Assam, India. Journal of Herbal Medicine and Toxicology. 5(2):65-72, 2011.

23. Kaur R, Sharma A, Kumar R, Kharb R. Rising trends towards herbal contraceptives. Journal of Natural products and Plant Resource. 1(14):5-12, 2011.
24. M. M. Pandey, S. Rastogi, and A. K. S. Rawat, "Indian herbal drug for general healthcare: an overview," The Internet Journal of Alternative Medicine, vol. 6, no. 1, p. 3, 2008.
25. M. P. Nair and A. R. K. Shastry, Eds., Red Data Book of Indian Plants, Vol-I, 1987, Vol-II, 1988, Vol-III, 1990, Botanical Survey of India, Calcutta, India.
26. M.O. M. Tanira, A. K. Bashir, R.Dib, C. S.Goodwin, I. A.Wasfi, and N. R. Banna, "Antimicrobial and phytochemical screening of medicinal plants of the United Arab Emirates," Journal of Ethnopharmacology, vol. 41, no. 3, pp. 201–205, 1994.
27. Pokharkar RD, Saraswat RK, Kotkar S. Survey of Plants having antifertility activity from Western Ghat area of Maharastra state. Journal of Herbal medicine and Toxicology, 4(2):71-5, 2010.
28. Priya G, Sarvanan K, Renuka C. Medicinal Plants with Potential anti-fertility activity-A review of sixteen years of herbal medicine research (1994-2010). International Journal of Pharm Tech Research, 4(1):481-94, 2012.
29. R. P. Samy, S. Ignacimuthu, and A. Sen, "Screening of 34 Indian medicinal plants for antibacterial properties," Journal of Ethnopharmacology, vol. 62, no. 2, pp. 173–181, 1998.
30. Ravichandran V, Arunachalam G, Subramanian N, Suresh B. Contraceptive and its significance in traditional system of medicines. International journal of pharmaceutical sciences, 1-2, 1998.

31. S. N. El and S. Karakaya, “Radical scavenging and iron chelating activities of some greens used as traditional dishes in Mediterranean diet,” International Journal of Food Sciences and Nutrition, vol. 55, no. 1, pp. 67–74, 2004.
32. S.Nair, R.Nagar, and R. Gupta, “Dietary anti-oxidant phenolics and flavonoids in coronary heart disease,” Indian Heart Journal, vol. 48, p. 545, 1996.
33. Shah GM, Khan MA, Ahmad M, Zafar M, and Khan AA. Observations on antifertility and abortifacient herbal drugs. African Journal of biotechnology, 8(9):1959-64, 2009.
34. Shrivastava S, Dwivedi S, Dubey D, Kapoor S. Traditional Herbal Remedies from Madhya Pradesh used as Oral Contraceptives-A Field Survey. International Journal of Green Pharmacy, 1(1):18-22, 2007.
35. T. H. Debas, R. Laxminarayan, and S. E. Straus, “Complementary and alternative medicine,” in Disease Control Priorities in Development Countries, D. T. Jamison, J. G. Breman, A. R. Measham et al., Eds., pp. 1281–1291, Oxford University Press, New York, NY, USA, 2nd edition, 2006.
36. T. Rabe and J. Van Staden, “Antibacterial activity of South African plants used for medicinal purposes,” Journal of Ethnopharmacology, vol. 56, no. 1, pp. 81–87, 1997.
37. Trypanosoma brucei brucei infection in mice. Journal of Ethnopharmacology 30: 307 – 313.
38. V. P. Kamboj, “Herbal medicine,” Current Science, vol. 78, no. 1, pp. 35–39, 2000.
39. V. Subhose, P. Srinivas, and A. Narayana, “Basic principles of pharmaceutical science in Ayurv˘eda,” Bulletin of the Indian Institute of History of Medicine, vol. 35, no. 2, pp. 83–92, 2005.

40. B. Ballabh and O. P. Chaurasia, “Traditionalmedicinal plants of cold desert Ladakh-Used in treatment of cold, cough and fever,” Journal of Ethnopharmacology, vol. 112, no. 2, pp. 341–345, 2007.
41. B. Patwardhan, D. Warude, P. Pushpangadan, and N. Bhatt, “Ayurveda and traditional Chinese medicine: a comparative overview,” Evidence-Based Complementary and Alternative Medicine, vol. 2, no. 4, pp. 465–473, 2005.
42. Bahmanpour, S., Talaei, T., Vojdani, Z., Panjehshahin, M.R., Poostpasand, A., Zareai, S. and Ghaeminia, M, Effect of Phoenix dactylifera pollen on sperm parameters and reproductive system of adult male rats. Iranian Journal of Medical Sciences, 31(4): 208 – 212, 2006.
43. Balandrin, P.M. Klocke, J.A., Wurtele, E.S. and Bullinger, W.H., Natural plant chemicals: sources of industrial and medicinal materials, Science 228: 1154 – 1160, 1985.
44. Balasinor, N., Bhan, A., Paradkar, N.S., Shaikh, A., Nandedkar, T.D., Bhutanik, K. and Roy- Chaudhaury, M., Postnatal development and reproductive performance of F1 progeny exposed in utero to an ayurvedic contraceptive: Pippaliyadi yoga. Journal of Ethnopharmacology, 109: 406 – 411, 2007.