Review Article

Bio-prospecting for fertility in humans: An update on herbal therapy

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Abstract

A survey of plants with bioactive components that are critical in resolving fertility issues is discussed. The need to focus more on local herbs is highlighted while more scientific research is recommended in order to get the best in bioprospecting with regard to sexually related morbidities, at times ascribed to microbes, some other times not, even when a few are noted to work against sexual productivity. Nigerian herbs contain attractive active ingredients in the treatment of various fertility disorders. The present review investigates the current survey across the world and the possible application on a global scale as effective intervention. This review is to serve as a lead that will provide empirical guide in the establishment of a databank for a sustainable resolution of fertility diseases through herbs in developing countries.

***Keywords*:** Bioprospecting, fertility, humans, microbes, antifertility

Introduction

Sexually transmitted infections have been with mankind for ages. They are transmitted through the 3 major routes of sexual intercourse: vaginal, oral and anal (Amu & Adegun, 2015; Glynn et al., 2018). Most of the diseases fester more among the vulnerable like adolescents, the aged and the poor (Cuffe et al., 2016; Liu et al., 2015). Most secondary school adolescents in Nigeria lack in-depth knowledge about these diseases, their symptoms, and modes of transmission (Amu & Adegun, 2015).The very common ones in Nigeria are chlamydia, syphilis and gonorrhea (Keshinro et al., 2016). Sexually transmitted infections are also prevalent among the youths in South Africa (Francis et al., 2018). Many of these diseases are incited by uncommon microorganisms. For example *Waddlia chondrophila* a chlamydia-like bacterium has been reported to impact negatively on the semen, sometimes when another disease may be progressing in the case (Baud et al., 2020)

Phytochemicals are compounds derived from plants through diverse forms of release, mostly by extraction (Zhang et al., 2015). They are attractive and strategic products of bioprospecting with application in medicine (Vishnuprasad & Unnikannan, 2017), food safety, food processing, production and storage (Velazhahan & others, 2017). Phytochemicals accumulate in different parts of the plants, such as in the roots, stems, leaves, flowers, fruits or seeds (Alagbe, 2019; Ghasemzadeh et al., 2018; Rachkeeree et al., 2018). They have intervention functions such as detoxification of carcinogenic agents through the neutralization of free radicals and inhibiting enzymes that activate cancer expression (Mollakhalili Meybodi et al., 2017). The active ingredients are found in vegetables, fruits, cereal grains, and beverages such as tea and wine. Antioxidant and free radical scavenging effect is associated with a risk of many diseases (Adjimani & Asare, 2015; Saltos et al., 2015). There are documented proofs of their potential role in improved endothelial function and increased vascular blood flow (Boonla et al., 2015). Sometimes, oxidative stress is the route by which instability is attained in the level of antioxidants which can be remedied by supplements readily obtainable in phytochemicals (Goszcz et al., 2015).

A few fertility related morbidities like gonorrhea and syphilis are common among sexually active persons (Tsevat et al., 2017). Gonorrhea, caused by the bacterium, *Neisseria gonorrhea*, is one of the most common sexually transmitted infections in developing countries (Duplessis et al., 2015). Symptoms of this disease in men include burning or pain during urination, increased urinary frequency, discharges from the penis, red or swollen opening of the testicles

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(Tsoumanis et al., 2018). It can also infect the urethra in a man's penis. Untreated gonorrhea can cause sterility in men and lead to infection that causes severe lower abdominal pain and fever, and can result in sterility (Dela et al., 2019). Syphilis is another bacterial disease, caused by *Treponema pallidum*, that predominantly affects the genitals area. The agent enters the body through the skin, the mouth, or the anus during sex (Stamm, 2015). There may be symptoms of fever, headache, swollen glands, or rash on the palms of the hands or soles of the feet. Untreated syphilis can cause damage to the brain, heart, eyes, and other parts of the body (Peterman et al., 2015). Genital warts are small, flat, flesh-colored bumps. Genital warts are attributable to a lot of types of human papillomavirus (Park et al., 2015). The Human papilloma virus is associated with cancer of the vulva, anus and penis (de Martel et al., 2017; Hartwig et al., 2017). Testicular cancer starts in one or both of the testicles. The testicles are situated in the scrotum, the skin that hangs up beneath the penis (Cheng et al., 2018). Hormones and sperm are developed in the testicles.

Herpes

Herpes is caused by a virus. It produces groups of blister-like sores on the genitals about 2 to 14 days after a person is exposed to the virus. The sores will open and become painful, especially if they come in contact with urine. Even though the herpes sores may disappear, the virus is still present and the sores can return with little warning (Gnann Jr & Whitley, 2016). Most people infected with genital herpes express no symptoms making it possible to spread even to when there are no sores or signs of the disease (McQuillan et al., 2018)

Hepatitis

Hepatitis B is a liver disease caused by a virus carried in the blood, saliva, semen and other body fluids of an infected person (Seto et al., 2018). Like HIV, it is spread by sexual contact or sharing tools for drug administration. Symptoms may include tiredness, poor appetite, fever, vomiting, joint pain, hives, rash, or jaundice – a yellowing of the skin and whites of the eyes. Doctors prescribe bed rest for those with hepatitis B. Most people recover, but some become long-term carriers of the virus, and can spread it to others (Terrault et al., 2018).

Benign Prostatic Hyperplasia (BPH)

This is the enlargement of the prostrate gland which causes urinary difficulties. It is usually been over age 40 (BPH) causes bladder-outlet obstruction. An obstruction can lead to decompensation of the bladder with residual urine incontinence urinary tract infection, hematuria and renal failure (Foo, 2019). Signs may include benign prostrate hyperplasia urinary retention or difficult urinating weight loss, fatigue and general weakness (De Nunzio et al., 2020).

Prostrate Cancer

Prostate cancer, found in elderly men expresses as uncontrolled abnormal increase in the number and size of cells. Pain during and after ejaculation, acute illness with fever, weakness and malaise, pain in the lower back, rectal area or perianal area (Pernar et al., 2018).

The causes of prostate cancer are unknown but may include genetic predisposition hormonal influences dietary and environmental factors and infectious agents (Nguyen-Nielsen et al., 2019). Prostate cancer varies widely in biological behavior and metastatic potential. Many attempts have been made to control this ailment using phytochemicals (Hosseini & Ghorbani, 2015; Komakech et al., 2017; Salehi et al., 2019).

Disorders of the Testes

This is the incomplete or abnormal descent of one testicle or both testes into the scrotum with gentle pressure (Hutson et al., 2015). But a true undescended testicle cannot be brought down in this way. Ectopic testicle is associated with cryptorchidism when the inner thigh is stroked longitudinally a retractile testicle can be brought back up into the lnguinal canal by a hyperactive cremaster reflex. Cryptorchidism of both testes lose the ability to produce sperm (Fawzy et al., 2015; Virtanen & Toppari, 2015). *Laurus nobilis* extract has been proven to rectify cryptorchid patients(Akunna et al 2012) . The common vegetable, *Talinum triangulare* recorded success in restoring normalcy to undescended testes in Wistar rats(Ogundoyin and Sanwo 2019) *Anthocleista djalonensis* is known to be a source of intervention regarding sperm profile in Wistar rats, having been confirmed to have an androgen-like and anti-inflammatory effects and best effect on sperm count.(Ezirim et al 2020) just like the extracts of *Rubus apetalus*(Rosaceae)was able to bring back the fertility potentials in unilateral cryptorchid rats(Munyali et al 2020).

This is a congenital displacement of the urethral opening on the dorsal surface of the penis. The condition, may present with epispadias (Ahmad & Watkin, 2019). Sign and symptoms are painful, curved erection that makes sexual intercourse difficult or impossible, deviation of the urinary stream. All the afore-mentioned have the capacity to end up in infertility (Lazzeri et al., 2016).

Phytochemicals and the integrity of reproduction

A pro-fertility agent, Sanrego, is very common intervention in Asian countries in the search for the eradication of male infertility (Luthfi et al., 2017). The plant, also called *Lunasia amara* Blanco, with wide

diversity has been generally accepted as an alternative medicine (Kamaruzaman et al., 2018). for male who constitute about 50% of all global infertility cases(Agarwal et al., 2015). Nor-Raidah & Mahanem, (2015) also confirmed the efficacy of this plant in enhancing on the fertility and libido in male Sprague dawley rats. They also enhance semen quality and fertility in birds (Durape, 2007).

Sometimes, the nutrient status and load may be a determinant in the efficacy of the phytochemicals as enhancers of fertility. He observed improved semen parameters, including improvement in sperm vitality [the number alive]; morphology [shape provides better motility as abnormal shape suggests problems with the cell]; and sperm motility (Durape, 2007). Bello et al., (2017) had reported the potentials inherent in *Abelmoschus esculentus* (L.) Moench in the management of infertility.

Defective sperm function, a major expression of infertility in man has been corrected by the use phytochemicals (Oliveira et al., 2015). Sesame leaf intake can increase epididymal spermatocytes reserve, improving sperm quality and testicular parameters, thus improving fertility in adult male rats (Amini Mahabadi et al., 2013; Khani et al., 2013; Shittu & Shittu, 2012).

The use of medicinal plants to treat sexually transmitted diseases in Nigeria was reported by Ajibesin et al., (2011). This is because in most African settlements, access to modern medical facility is at a discount, making the traditional medical practitioners an attraction. The efficacy of herbal extracts in controlling sexually transmitted diseases and AIDS was further confirmed by (Lamorde et al., 2010).

Some plants have been exploited in the treatment of prevention of genital tract diseases and STIs, and through their antiviral and antimicrobial effects. They include *Taxillus, Aristolochia, Syzygium cumini, Albizia adianthifolia, Bidens pilosa, Carica papaya, Ranunculus, Peltophorum africanum, Vachellia karroo, Rhoicissus tridentate, Houttuynia cordata, Panax notoginseng, Nelumbo nucifera, Astragalus, Hypericum aethiopicum, Spondias mombin, Jatropha zeyheri, Ximenia caffra, Trichilia dregeana, Clematis brachiate, Tabernaemontana, Sarcophyton* (Ajibesin et al., 2011; Chinsembu, 2016; Gbadamosi, 2014; Jadhav et al., 2015; Mamba et al., 2016; Naidoo et al., 2013; Nazer et al., 2019; Paniagua-Zambrana et al., 2020).

Apple vinegar is a very strong antibiotic and disinfectant agent, and its antibacterial and antifungal properties boost the immune system of the body against microbial intruders (Saqib, 2017). Oak tree bark and leaves contain tannin, sugar, gallic acid, malic acid, quercetin, mucilage, pectin, resin, and oil. Therefore, this plant has a very strong antibacterial property and produces strong effects in reducing and treating genital tract bacterial diseases and STIs (Nazer et al., 2019).

Soma is known as one of the effective traditional and herbal drugs as well as a home remedy for STDs due to its potent antibacterial properties (Nazer et al., 2019). Leaves, tree bark, roots, and fruit of soma have high pharmaceutical value, and its anti-inflammatory and antibacterial properties help fight certain diseases like gonorrhea and syphilis. In addition, soma contains saponin, which consists of phytochemicals (plant chemicals) that help kill all types of germs, boost the immune system, and restore the body (Nazer et al., 2019). Dülger et al., (2002) reported the control of Herpes simplex by the extract of *Verbascum phlomoides* L, while Shikalange et al (2016) exploited the active ingredients of Acacia *karroo* and *Rhoicissus tridentata* subsp. *cuneifolia* and concluded they were are potential candidates to treat venereal diseases (Tshikalange et al., 2016).

Silybum marianum is also one of the herbal drugs that are used for treating STDs with traditional form of medicine. The *S. marianum* is rich in silymarin (a natural material that can destroy T. vaginalis), which makes the plant an ideal choice to fight against certain types of STDs (Nazer et al., 2019). In addition, this substance is also used to boost the immune system of the body and therefore helps fight the parasite that causes infection in the body (Wilasrusmee et al., 2002).

Plants like *Achyranthes aspera* L., *Lannea discolor* (Sond.) Engl., *Hyphaene petersiana* Klotzsch ex Mart., *Asparagus racemosus* Willd., *Capparis tomentosa* Lam., *Cleome hirta* Oliv., *Garcinia livingstonei* T. Anderson, *Euclea divinorum* Hiern, *Bridelia cathartica* G. Bertol., *Acacia nilotica* Delile, *Piliostigma thonningii* (Schumach.) Milne-Redh., *Dichrostachys cinerea* (L.) Wight and Arn., *Abrus precatorius* L., *Hoslundia opposita* Vahl., *Clerodendrum capitatum* (Willd.) have been successfully used as effective interventions against STDs (Chinsembu, 2016). A healing action on genital herpes by Aloe vera was reconfirmed by (Maan et al., 2018; Syed et al., 1997). Vermani & Garg, (2002) reported interventions of herbal origin which possess activity to prevent and treat STDs including AIDS, vaginal and topical applications.

Aphrodisiacs

Any agent with the ability to provoke sexual desire in an individual is referred to as an aphrodisiac (West & Krychman, 2015). Aphrodisiac plants are used in the treatment of erectile dysfunction (ED) in men (Lim, 2017).

Carpolobia plant is very common in West and Central Africa among the Pygmies of Cameroon. It is an accepted and commonly utilized herbal booster of libido (Nwidu et al., 2015). It is used to cure male infertility and to boosts libido and also used to induce penile erection, and enhance male virility. The chewing stick prepared from the stem and root of

Carpolobia alba (CA) or *Carpolobia lutea* (CL) is patronized because it boosts male sexual performance (Akinola et al., 2020). The genus *Carpolobia* has over 14 species. The leaf essential oil contains a variety of terpenoids, while polyphenols and triterpenoid saponins have been isolated from the root and leaf extracts respectively (West & Krychman, 2015). Other ethnomedicinal uses include curing of stomach ailments, rheumatism, fever, pains, insanity, dermal infection, venereal diseases; to promote child birth; and as a taeniafuge and vermifuge (Nwidu et al., 2015). In spite of its registered aphrodisiac potentials, its importance is restricted to the locals of the coastal south east Nigeria and West Africa. The Efiks, an ethnic group in Nigeria, use this plant as chewing stick to enhance libidinal profile of their men which is also confirmed to induce of penile erection; enhancement of aphrodisiac prowess; enhancement of virility and male fertility; and augmentation of male sexual functions (Nwidu et al., 2015; Olayinka et al., 2019).

Screening of the root and leaf extracts revealed the presence of tannins, saponins, flavonoids, cardiac glycosides, anthraquinones, and terpenes, triterpenoid saponin and polyphenols (Sengupta et al., 2012).

Epilobium sp. Biological or pharmacological screening of the substances of potential health benefits, for example anti-aging or chemo preventive activity and their phytochemical profiling, should be systematic and of wide range (Stolarczyk et al., 2013). Recently, there was a growing interest in members of the genus *Epilobium* sp. (family Onagraceae) consisting of nearly 185 species worldwide. Biological or pharmacological screening of the substances of potential health benefits, for example anti-aging or chemo preventive activity and their wide ranging phytochemical profiling, have been systematically carried out (Stolarczyk et al., 2013). Chemical analyses had indicated the presence of alkaloids, glycosides, tannins, and flavonoids in the crude ethanolic extract most of which are known to possess potent antioxidant activity. The results of antioxidant activity indicate higher free radical scavenging activity (Onar et al., 2012).

Anti-fertility

In spite of their benefits as fertility enhancers, bioprospecting revealed that plant chemicals also act as anti-fertility agents (Sharma et al., 2013). For example the screening and evaluation of anti-fertility activity of *Dactyloctenium aegyptium* in male albino rats decreased levels of sperm count, weight of reproductive organs, serum hormonal levels and number of implantations in female rats reveals the antifertility activity in a dose dependent manner (Naik et al., 2016). Gupta et al., (2011) reported the antispermatogenic activity of *Thevetia peruviana.* Phytochemical examination showed that this plant is rich in active constituents, like α-amyrin acetate, lupeol acetate, α-amyrin, β-amyrin, lupeol and thevetigenin (Bhagour et al., 2015; Gupta et al., 2011). When the stem bark methanol extract was administered orally to male rats at the dose level of 100 mg/rat/day no significant reduction in body weight was noted, while the weight of reproductive organs reduced significantly. A significant fall in the total protein and sialic acid content of the testes was also observed confirming the extracts an active contraceptive (Gupta et al., 2011).

Prospect

In choosing any herbal remedy, the efficacy is measured with respect to high level of direct inactivation and control of the microbial agents and the low level of side effects on the human cells. Many herbs have been embraced by indigenous populations for regular treatment of STIs. Even with the drawback of lack of expiry date, inconclusive dosage, crude nature of active ingredients, and overall compromised standards, herbal interventions still find a place in the heart of man and cannot be overlooked by the World Health Organization (WHO).

It is therefore advised that more involvement of the rural populace is factored into continuous studies and investigation on plant and their products for human health. Analytical laboratories must recognize the need for active collaboration and inclusiveness with those whose lives have been sustained on crude interventions. Their contributions may be the relevant information needed to fully accept and standardize herbs and their extracts in the treatment of sexually transmitted infections, even when till date, which guidelines for treatment are not yet in agreement with current varied crude preparations.

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