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An overview of phytosomal treatment for PCOS

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Abstract
Polycystic ovarian syndrome (PCOS) is a prevalent hormonal disorder affecting women of reproductive age. It generally begins in youth, but symptoms might vary with time. PCOS can cause hormonal abnormalities, irregular menstrual cycles, elevated androgen levels, and ovarian cysts. Irregular periods, generally due to a lack of ovulation, might make it difficult to conceive. PCOS is the major cause of infertility. PCOS is a chronic disorder that cannot be healed. However, certain symptoms can be alleviated with lifestyle modifications, drugs, and fertility treatments. Phytosomes are complexes of phospholipids and naturally active phytochemicals bound in their structures, formed by the interaction of phosphatidylcholine (or any hydrophilic polar head groups) with plant extracts in an aprotic solvent. Phytosomes with balanced hydrophilicity and hydrophobicity may easily pass the bilipid cell membrane, increasing the bioavailability and absorption of water-soluble plant metabolites and boosting therapeutic efficacy. Phytosomes are safe to use and affordable in cost. There are two ways for preparing phyto-phospholipid complexes: solvent evaporation and anti-solvent precipitation. Solvent evaporation is a common process for producing phospholipid complexes, including phytosomes. Characterisation of Phytosomes Their characterization is based on physical properties such as form, size, distribution, drug, and chemical content.Phytosomes have several benefits, including improved medication absorption, anti-cancer and antioxidant properties, transdermal drug delivery, and wound rejuvenation.

Keywords: Chhani, consumption, fuel-wood, households, Lanchaan

Introduction

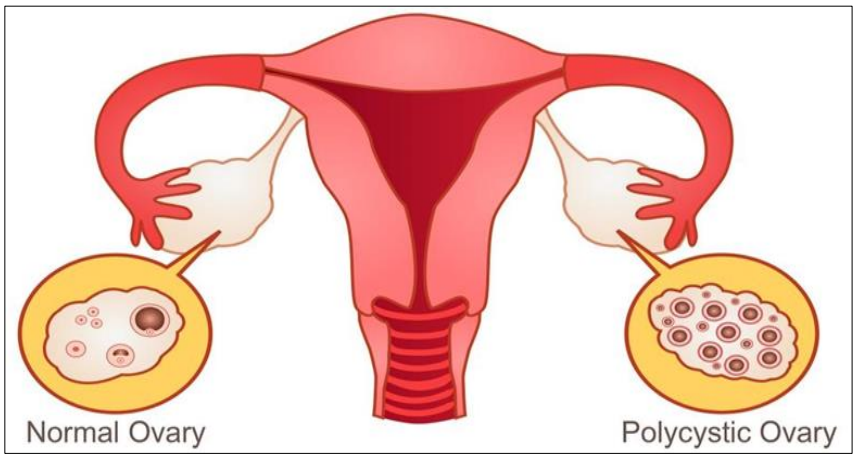

Fig 1: Polycystic Ovaries Syndrome

Polycystic ovarian syndrome (PCOS) is an endocrinological illness that affects the anatomy of the ovaries and causes metabolic problems in females. According to the Rotterdam ESHRE/ASRM (2004) criteria, it is a hyperandrogenic condition characterised by persistent oligoanovulation and ultrasonographically confirmed polycystic ovarian morphology [1]. Disrupted androgen levels and synthesis pathways, together with insulin resistance, are the major causes of psychological impairments such as depression and other mood disorders, as well as metabolic abnormalities [2].

Females with obesity or overweight are reported to have impaired metabolic and reproductive activities, leading to the PCOS phenotype. There main three symptoms to identify PCOS: irregular cycles, hyperandrogenism, and polycystic ovary morphology (PCOM) [3]. Polycystic ovary syndrome has diagnosis rate of females who have this syndrome can be 6-20%, based on the population [4]. According to one study, 35% of mothers and 40% of sisters of premenopausal untreated PCOS patients have the condition, demonstrating the role of heredity. Global Prevalence A growing body of research suggests that higher Gonadotropin-releasing hormone (GnRH) pulse frequency and amplitude might favour Luteinizing hormone (LH) production over Follicle stimulating hormone (FSH) synthesis, resulting in a high LH/FSH ratio in women with PCOS [5, 6].

According to the findings shown below, elevated LH levels play an important role in the development of reproductive and metabolic diseases. First, LH stimulates the production of androgen in ovarian theca cells, resulting in hyperandrogenemia and stalled follicle growth [7]. Second, increasing LH pulse frequency reduces oestrogen and FSH production, which prevents follicle expansion and ovulation. Third, LH stimulates ovarian release of Insulin-like Growth Factor-1 (IGF-1), which can further enhance LH binding and androgen synthesis in theca cell, ultimately contributing to the development of polycystic ovaries in PCOS patients [8]. However, it is still unclear whether the aberrant GnRH function is fundamental malfunction of the hypothalamus and pituitary or secondary to the complex influence of reproductive and metabolic disorders, as well as an imbalanced immune system. In PCOS patients' intestinal microenvironment. There are no particular tests for PCOS diagnosis. Therefore, a careful differential diagnosis plays a relevant role. Pelvic examination, a transvaginal ultrasound, and sex hormone levels measurement associated with a careful medical history, including weight changes and related insulin resistance symptoms, are the most commonly recommended investigations [9, 10, 11].

Introduction to drug

Fig 2: Orchid Tree (*Bauhinia variegata*) in Full Bloom

Many herbal medications play an important role in illness treatment. *Bauhinia variegata*, also known as Kanchanar, is a tree with numerous therapeutic benefits that have long been used in Ayurveda. It may be found in the subcontinent's tropical and temperate areas [12]. Kanchanar is used to treat PCOS in the form of Kanchanar Guggul. It is a helpful treatment for a variety of illnesses, including PCOS, uterine cysts, many joint aches, and hormonal imbalances. 'Guggulu' is the Sanskrit name for Guggul, which meaning 'protect against illnesses'. Guggul also helps to remove toxins from the body, which improves the functioning of the lymphatic system. Kanchanar guggul contains the following herbs: Varuna, black pepper, and long pepper. Kwath of Triphala, pure Guggul resin, cardamom, and cinnamon [13, 14]. Several investigations have shown that Kanchnar has antidiabetic, anti-oxidant, analgesic, anti-dyslipidemia, anti-inflammatory, anti-microbial, cytotoxic, and anthelmintic activities. Bark juice is used to treat amoebic dysentery, diarrhoea, and other stomach ailments. The bark paste is excellent for treating cuts and wounds, skin problems, scrofula, and ulcers. It may also be used to treat coughs, asthma, and abdominal distention, as well as to gargle sore throats and protect against skin illnesses. It is effective in treating skin discolouration. Researchers have also demonstrated that Kovidar has anti-diabetic, cytotoxic, fibrolytic, antiinflammatory, anti-arthritic, anti-diarrheal, and antibacterial properties [15, 16].

Introduction to phytosomal intravaginal gel

The prefix "phyto" refers to plants, and "some" denotes cell-like [17]. Phytosome is a method for creating lipid-compatible molecular complexes of medicines and nutraceuticals, standardised plant extracts, or water-soluble phytoconstituents to improve absorption and bioavailability. It is sometimes called herbosomes [18]. Phytosome is a new developing technology for phytopharmaceuticals that comprises phytoconstituents encapsulated in plant extracts and bonded by lipids [19]. Phytosomes are herbal formulations that improve the therapeutic benefits of plant extracts and herbal lead molecules by improving their bioavailability in the target site as compared to standard herbal extracts. This is an enhanced kind of herbal formulation in which the bioactive phytoconstituents of herb essence are contained and bonded by a lipid [20, 21].

Intravaginal administration is the process of introducing a drug into the vagina. The typical vaginal pH for healthy women of reproductive age ranges from 3.8 to 4.2 [22]. The primary benefit of this method of administration is that illnesses and disorders of the vagina may be treated locally, delivering a high concentration of medicine at the site of disease and perhaps reducing any harmful effects outside of this region [23]. There are several illnesses and ailments that require a medicine to be administered intravaginally, as well as preventative and fertility-promoting uses, and multiple drug delivery devices are now in use, such as vaginal gels, pessaries, and intravaginal rings. The procedure of delivering a vaginal gel is less familiar for the patient than, say, taking a pill. Oral suspension. Furthermore, following administration, gel formulations may be noticeable to the patient or interfere with other activities, such as coitus, leading to an unwillingness to use a product. Thus, the sensory experience of utilising intravaginal products is critical in ensuring patient adherence and compliance with the treatment [24].

Intravaginal medication administration can provide a local impact or deliver medicines systemically, bypassing hepatic first pass metabolism. The advantage of these dose forms is that they allow the medicine to remain in the vagina for an extended period of time, eliminating the need for regular dosing. There are various typical dose formulations for intravaginal medication administration [25]. Gels and creams are popular semisolid dosage forms used to administer drugs over short periods of time and with repeated application.

Suppositories/pessaries are also available; they are commonly labelled as "ovules" and are often made of glycerol-gelatin bases; PEGs and fatty bases are prone to cause discomfort. Intrauterine devices or vaginal rings can be used to give drugs over lengthy periods of time [26, 27].

Diagnosis and treatment

PCOS diagnosis requires at least two of the following three elements: hyperandrogenism, ovulatory dysfunction, and PCOM [28]. Obesity is frequent, however it does not always imply the existence of the condition [29]. Hyperandrogenism is classified into two categories: biochemical and clinical. Biochemical hyperandrogenism is defined as mild to moderately high blood levels of androgenic precursors such as dehydroepiandrosterone Sulphate (DHEAS), androstenedione (A4), and appropriate forms of androgens such as testosterone (T4) [30]. The major clinical symptom of hyperandrogenism is hirsutism, while alopecia and acne are minor clinical indications [30, 31]. Clinically, ovulatory dysfunction manifests as amenorrhoea, or the lack of menstruation. The polycystic ovarian morphological context includes ultrasound scans with more than 12 follicles per ovary, and/or more More than 20 follicles in both ovaries, with an ovarian volume of at least 10 cm3 [28]. Primordial follicles develop into preantral and antral follicles, resulting in PCOM [32, 33]. LH, FSH, and estradiol levels have an additional role in diagnosing [32]. The increased LH to FSH ratio is particularly relevant due to the increased gonadotropin hormone-releasing hormone (GnRH) pulse frequency, which indicates the existence of the syndrome [32, 33]. Excess LH and ovarian androgens, as well as excess LH stimulation, are the primary causes of this condition [32, 34].

Treatment alternatives are examined differently for each patient due to diverse pathways and phenotypes. Furthermore, it is important to understand that lifestyle has a significant influence on pathogenesis. Modifications in everyday living can assist with overall symptom management [35]. Exercising frequently and eating a healthy diet can help lower BMI. Combined oral contraceptives (OCs) are the first-line medicines used to treat PCOS. They are composed of oestrogen and progesterone. They primarily control menstruation and reduce the severity of hyperandrogenism symptoms [36]. Antiandrogens are a class of medicines that compete for androgen receptors and decrease their effects. Ovulation inducers are an effective therapy for anovulatory sterility caused by PCOS. Clomiphene citrate is a first-line treatment for ovulatory disorder. Competitively binds to oestrogen receptors at the brain and pituitary level, reduces the negative feedback effect of oestrogen, and raises FSH [37]. Omatase inhibitors are also beneficial for ovulatory dysfunction because they block T4 conversion to estradiol, resulting in positive feedback on the hypothalamic-pituitary-ovarian axis. This positive feedback leads to GnRH production, followed by FSH release and follicular stimulation [38].

Table 1: Different additives used in the formulations of phytosomes

Compound	Examples	Role
Phospholipids [39]	Soya phosphatidyl choline, Egg phosphatidyl choline, Dipalmityl phosphatidyl choline, Distearyl phosphatidyl choline, soya lecithin, cholesterol	Enhance bioavilability of active constitute
Aprotic solvents [40]	Dioxane, acetone, methylene chloride, dichloromethane.	Phytosomes lipid vesicles
Non solvent [41]	n-hexane and non-solvent i.e. aliphatic hydrocarbon	Phytosomes lipid vesicles
Alcohol [42]	Ethanol, Methanol	Enhance drug carrier loading capacity

Methods for Phytosomes preparation

Antisolvent precipitation technique

The medication and cholesterol (1:1) were combined in a 100 ml round bottom flask and refluxed with 20 ml of dichloromethane at 60℃ for 2 hours. The liquid was then concentrated to 5-10 ml. Hexane (20 ml) was carefully added while stirring continuously to produce the precipitate, which was then filtered, collected, and kept in vacuum desiccators overnight. The dry precipitate is crushed in a mortar and sieved through #100 meshes. The powdered compound was placed in an amber-colored glass container and kept at room temperature [43].

Solvent evaporation method

The medication and cholesterol (1:1) were combined in a 100ml round bottom flask and refluxed with 200 ml of acetone at 50-60℃ for 2 hours. The precipitate was then filtered and collected.The dried precipitate phytosomes complexes were put in an amber-coloured bottle [44].

Evaluation of phytosomes

Visualisation

The morphology of phytosomes was studied using a digital microscopy transmission microscope and a scanning microscope.

Digital microscopy; Shake the phytosome formulation in water and observe it under a digital microscope with a 400X objective lens.

TEM analysis

The complex was shaken in water and examined using a Transmission Electron Microscope (Hitachi, Japan).

SEM analysis

Approximately 5 µL of phytosomal solution was converted into a canopy slip, which was then mounted on a specimen tab. The samples were left to dry at temperature. The particle size of the formulation was then examined and photographed using a scanning microscope (Sigma scan, Carl Zeiss scan). The particles were coated with platinum under vacuum pressure, and the coated samples were examined and photographed using the JEOL JSM-6701F emission SEM.

a) Particle Size Analysis Beckman Coulter's DelsaTM Nano measured particle diameter and polydispersity index. Phytosome preparations were diluted with methanol and assessed.
b) FTIR. Spectral data were collected to determine the structure and chemical stability of extract, PC, and phytosome. Spectral scanning was exhausted in the region of 4000 to 5000 cm.

c) DSC The sample including phospholipons and phytosomes was put in an aluminium crimp cell and heated at 100C/min from 0 to 4000*C in a nitrogen environment (TA Instruments, USA, Model DSC Q10 V24.4 Build 116). The peak transit time onset temperatures were recorded using an analyzer [45].

Advantages of phytosomes

1. It facilitates proper medicine delivery to certain tissues.
2. Using phytosomes to distribute herbal extracts doesn't jeopardise their nutritional safety.
3. Increased absorption of minor elements has reduced the required dosage.
4. The drug's bioavailability improves dramatically.
5. The medication's conjugation with lipids creates vesicles, resulting in a high and excessively specified entrapment capacity.
6. There are no concerns about drug entrapment in phytosome formulations. Phytosomes create high stability profiles due to the formation of new chemical interactions between phosphatidylcholine molecules and herbal phytoconstituents.
7. Phosphatidylcholine serves as both a transporter and a nutrient in phytosomes.
8. Phytosomes have significant clinical benefit.

Disadvantage of phytosomes

1. Phytosomes have the potential to quickly eliminate phytoconstituents, resulting in overall advantages.
2. Phospholipids can increase proliferation in the MCF-7 breast cancer cell line.
3. Phytosomes are limited by the leaching of phytoconstituents, resulting in decreased medicine concentrations.

Application of phytosomes

1. Improving bioavailability first.
2. Provision of large and diverse pharmaceuticals, including proteins and peptides.
3. Secure arrangement.
4. Hepatoprotective.
5. Accepted for Use in Pharmaceutical and Cosmetic Applications.
6. Minimal risk profile.
7. The properties of toxicity have been well-documented.
8. Attractiveness to the market.

Conclusion

Phytosomes, also known as herbosomes, are advanced and innovative forms of botanicals and phyto-constituents that are more readily absorbed orally, topically, and transdermally. Phytosomes have better pharmacological characteristics and a wide range of applications in cosmetics. The procedures for preparing phytosomes are unconventional, easy, and repeatable. Aside from that, the phospholipids utilised have their own positive effects on the body. Several regions of phytosomes will be described in the future for pharmacological applications. The phytosome technique connects the classical delivery mechanism of phytoconstituents to innovative medication delivery technologies. An attempt was made to investigate more study into phytosomes and their uses, such as wound healing, antioxidant, and anti-cancer properties. The information acquired below will be valuable for the researchers. Who want to investigate a vesicular drug delivery method that includes an effective medication on the track site without requiring metabolism. Phytosome technology should be developed to treat various neurological, cardiovascular, and auto-immune illnesses, as well as skin ailments. Although numerous phytosome products are currently on the market, many additional phytoconstituents with outstanding potential to treat life-threatening disorders have yet to be integrated into phytosome technology. Further research is frequently conducted to generate extremely target-specific phytosomes.

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