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DEVELOPMENT AND CHARACTERISATION OF POLYHERBAL PHYTOSOME GEL FOR DERMOCOSMETIC APPLICATIONS

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ABSTRACT

Novel drug delivery system is a new approach to drug delivery the shows the limitations of the traditional drug delivery system. The effectiveness of any herbal medication is depend on the delivery of effective level of the therapeutically active compound. Therefore, phytosomes are recently introduced herbal formulations that are better absorbed and as a result they produce better bioavailability than the conventional phyto-molecules or botanical extracts. The aim and objective of the study is to develop polyherbal phytosome gel for dermocosmetic application using Couroupita Guianensis andCassia Fistula extract. The phytosome are prepared by reflux method and were optimized. The formulations of phytosomes were analyzed for measurement of particle size & zeta potential, drug content, drug entrapment efficiency, percentage yield, in-vitro drug release studies and Exvivo permeation study.Then incorporate this phytosomal complex into gel formulation. Polyherbal phytosome gel formulation were evaluated by spreadability, drug content, measurement of pH, homogeneity, rheological studies.[1]

KEYWORDS: *novel drug delivery system, phytosomes, couroupita guianensis,cassia fistula,polyherbal phytosomal gel*

INTRODUCTION

Phytosomes

Phytosomes are a novel and advanced form of herbal extracts that are designed to enhance the absorption and bioavailability of phytoconstituents found in plants. The term "phytosome" is derived from the Greek word "phyto," meaning plant, and "soma," meaning body or cell. It refers to a complex composed of a phytoconstituent or plant extract and a phospholipid molecule.

Phytosomes are created through a specialized process known as phytosome technology, where the phytoconstituents are combined with phospholipids, usually derived from soybeans or sunflower oil. Phospholipids are natural substances found in cell membranes, and their structure allows them to form a complex with the phytoconstituents, improving their solubility in both water and fat. This unique structure enhances the absorption and delivery of the active compounds to the target cells and tissues.

The formation of phytosomes helps overcome the limitations of conventional herbal extracts, which often have poor solubility in water and limited absorption in the body. By attaching the phytoconstituents to phospholipids, phytosomes are able to mimic the body's natural cell membranes, facilitating their transportation across biological barriers.

The benefits of phytosomes include improved bioavailability, enhanced absorption, increased stability, and targeted delivery of the active compounds to specific tissues or organs. Phytosomes have been extensively studied and utilized in various areas, including nutraceuticals, cosmetics, and pharmaceuticals.

Structure of Phytosomes

Phytosomes are complex of phospholipids and active phytochemicals ,bound in their structure obtained by the reaction between phosphatidylcholine(or any hydrophilic polar head groups) and plant extracts in an aprotic solvent.

Applications of phytosomes:

- Hepatoprotective eg:Silymarin phytosomes
- Antioxidant eg:green tea phytosome, grape seed phytosome
- Anti carcinogenic property eg: grape seed phytosome

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- Anti mutagenic property eg: grape seed phytosome.
- Anti inflammatory activity eg; curcumin cholesterol phytosomal complex
- Immuno modulatory eg: Echniacea phytosomes[1]b)GELS

Gels are semisolid preparation intended for use on the skin or the mucous membrane. This is a semi-rigid structure in which the movement of dispersing medium in dispersed phase is limited by an interweaving three-dimensional system of particles. Vast quantities of watery or hydro alcoholic fluid are entangled in a system of colloidal solid particles which may comprise of organicpolymers from synthetic or natural origin or inorganic substance.

Structure of Gels

The gelling agent which forms network by interlinking particles results in the rigidity of gel. Type of force which causes the linkage of particles and its nature govern the arrangement of system and gel properties. The single particles show isometric aggregates or spherical cluster of minute molecules or solomacromolecules.

Applications of Gels

- Used in soft and hard gel pills.
- Preparation of suppositories: Glycerin in suppositories BP.
- Gels are used to create continuous release formulation.
- Used for drug administration to various routes such as tropical,intranasal, intraocular, vaginal, rectal andintramuscular and parenteral in some cases.
- They are widely used in food and cosmetic industry.
- Phosphoric acid and sodium fluoride gel used in dental care.

ACTIVITIES

Uses of *Couroupita Guianensis*

Antioxidant activity: It has long been recognised that naturally occurring substances in higher plants have antioxidant activity. Among those substances, the flavonoids that are widely distributed in plants have the ability to scavenge free radicals, superoxide and hydroxyl radicals by single-electron transfer. An antioxidant exerts its antioxidant activity through various mechanisms, including chelating ferrous iron, degrading peroxide, and scavenging free radicals. In our experiments, the antioxidant activity of *Couroupita guianensis* has been investigated by a DPPH radical scavenging activity[2].

Antitumor activity:The leaf of *C. guianensis* consists of isatin compound that has cytotoxicity against human carcinoma cell lines.It has the potential to be used as a chemotherapeutic agent against cancer. Isatin isolated from floral parts exhibited cytotoxicity against HL60 cells

Anti bacterial activity:*C. guianensis* shows good antimicrobialactivity but low antimycobacterial activity. The plant extract of *C. guianensis* is equipotent to standard drugs such as paracetamol in its analgesic activity and indomethacin in its anti-inflammatory activity.

Anti inflammatory:The outcomes display that *Couroupitaguianensis* fractions have anti-inflammatory effect, partly due to a reduction on cell migration and inhibition on cytokines and inflammatory mediators production

Anti fungal:Indirubin is one of the important chemical components of *C. guianensis* which is used as an antifungal agent, particularly to cure fungal diseases, dermatophytic and skin lesion diseases. It is active for the treatment of chronic myelocytic leukemia[2]

Other activities:it will shows anti ulcer, anti diabetic, anti emetics

Uses of *Cassia Fistula*

Anti bacterial:in *Cassia fistula*, the distilled water, acetone and ethanolic extracts of leaves show excellent antimicrobial activity against Gram negative bacteria i.e., E. coli and only distilled water and ethanolic extracts are found to be inhibitory for Gram positive bacteria i.e., Bacillus subtilis

Anti fungal:The in vitro findings justify the use of *Cassia fistula* in traditional medicine practice for the treatment of some fungal infections. However, study on the toxicity of the crude extracts and the compounds isolated from this plant should be assessed to ensuretheir eligibility to be used as sources of modern medicines.

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Laxative: *Cassia fistula* is widely used in traditional Persian Medicine as a mild laxative. The rate of chronic constipation increases above the age of 60.

Anti oxidant:The order of antioxidant activity in *Cassia fistula* extracts displayed from higher to lower level as methanolic extracts of pulp, methanolic extracts of seed, hexane extracts of pulp, and hexane extracts of seed

Other activities: *Cassia fistula L* possess hepatoprotective and antitussive characteristics. It contains antibacterial and antifungal properties. Cassia fistula L is used for healing of wounds and gastrointestinal illness. It is an excellent source of glycosides, tannins,and flavonoids

MATERIALS AND METHOD

Extraction methods of Couroupita Giuanensis

Decoction extraction method:For the decoction, method was followed as previously used by Li et al., 5 g of dried powder was extracted with 100 mL of deionized water at 100°C for 30 min in a water bath.

Ethanolic Maceration Extraction Method: For the ethanolic maceration, method was followed as previously used by An,5 g of dried powder was extracted with 100 mL of 50% aqueous ethanol at 25 °C for 42 h in static condition.

Methanolic Maceration Extraction Method: For methanolic maceration, method was followed as previously used bycai et al.55, 5 g of dried powder was extracted with 100 mL of 80% aqueous methanol at 35°C for 24 h in an incubator .

Cold Percolation Method: For cold percolation extraction, method was followed as previously used by Parekh and Chanda56, 10 g of dried powder was taken in 150 mL petroleum ether in a conical flask, plugged with cotton wool and then kept on a rotary shaker at 120 rpm for 24 h.After 24 h, it was filtrated through eight layers of muslin cloth and the solvent was evaporated from the powder. This dry powder was then taken in 150 mL of deionized water and was kept on a shaker at 120 rpm for 24 h.

Microwave Assisted Extraction Method: For microwave assisted extraction, method was followed as previously used by Jaitak et al.57, 1 g of dried powder was extracted with 200 mL of deionized water in a conical flask in a microwave(Magicook 20S (Galaxy), India) at different power levels ranging from 20-160 W with extraction time range between 30 sec to 5 min with a temperature range of 10-90EC.

Infusion Extraction Method: For infusion extraction, method was followed as previously used by Martins et al.58, 2 g of dried powder was extracted with 400 mL of boiling deionized water and were left to stand at room temperature for 5 min[5].

Soxhalation method:*Couropita guianesis* leaves was successively extracted by using the Soxhlet assembly taking the different solvents such as Petroleum ether, Chloroform and Methanol based on the increasing polarity. All the extracts were evaporated to remove excess of solvent in a water bath. These extracts were then stored in air tight container at cold temperature (approx. 15oC)[6].

Extraction of *Cassia Fistula*

Maceration:5g petals of flower dried under shade was made into a paste in a mortar. The paste obtained was stirred with 50mL of organic solvent for nearly 3 hours, using a magnetic stirrer, in an Erlenmeyer flask. The yellow colored solution was decanted and the residue was again extracted twice with the same solvent.The extracts were combined together and concentrated in a rotary evaporator. The dried mass is collected and used as such for GC MS analysis and for antioxidant assay. The solvents used are dichloromethane, ethyl acetate and n-hexane.

Soxhalation method:The flowers of *C.fistula* were dried in shade and powdered in a mechanical grinder. The powder(25.0gm) of the plantmaterials were initially de-fatted with petroleum ehrer (60- 80°C), followed by 900 ml of hydroalcoholusing a Soxhlet extractor for 72 hrs at a temp. notexceeding the boiling point of the solvent. The extracts were filtered using Whattman filter paper (No.1), while hot and concentrated in vacuum under reduced pressure using rotary flask evaporator and dried in a desiccator. The hydroalcoholic extract yield a dark brownish solid residue weighing 6.750 gm (27.0%w/w) respectively. the extracts were kept in sterile bottles, under refrigerated conditions, until further use.The dry weight of the plant extracts was obtained by the solvent evaporation and used to determine concentration in mg/ml. the extract was used directly for DPPH assay, total phenol and ferrous reducing power content and also for assessment of antioxidant capacity through various chemical assays[7]

FORMULATION OF PHYTOSOMES

phytosomes can be prepared by REFLUX METHOD:

The specific amount of cassia fistula, couroupita guianensis extract and soya lecithin were placed in a 100 ml round bottom flask

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and 50ml of methanol was added as reaction medium. The mixture was refluxed and the reaction temperature of the complex was controlled to 50 °C for 3 hrs. The resultant clear mixture was evaporated and 20 ml of N- hexane was added to it with stirring. Theprecipitated was filtered and dried under vaccum to remove the traces amount of solvents. The dried residues were gathered and placed in dessicators and over night and stored at room temperature.

EVALUATION OF PHYTOSOMAL COMPLEX

1 . **Microscopic view**

Optical microscopy was used for characterization of the complex. The complex was suspended in buffer and a drop was placed on a slide and covered with a cover slip. Microscopic view of the complex was observed at a magnification of 45X[9].

2. Percentage Practical Yield

Percentage practical yield was calculated to know about percent yield or efficiency of any method, thus its help in selection of appropriate method of production[10].

Phytosomes prepared were collected and weighed to determine practical yield from the following equation:

(%) Yield = (Practical yield) × 100 (1)(Theoretical yield)

3. Entrapment efficiency

100 mg of phytosomal complex were centrifuged at 2000 rpm for 30 min using a Remi centrifuge to separate phytosomes from un entrapped drug. Concentration of the free drug as the supernatant was determined by measuring absorbance at 279nm using UV-Visible spectrophotometer[11]. The percentage drug entrapment was calculated by using the formula,

Entrapment efficiency (%) = (Total amount of drug) – (amount of free drug) × 100/Total amount of drug

4. Drug content

Phytosomes equivalent to 10 mg of drug was accurately weighed and taken into a 100 ml volumetric flask. The contents of the flask was dissolved in small quantity of ethanol and sonicated for 30 minute. Volume was adjusted to 100 ml with ethanol. Contents of the flask were filtered and drug content was determined spectrophotometrically using UV spectrophotometer after appropriate dilutions[9]

5. Scanning Electron Microcopy (SEM) Analysis:

To detect the surface morphology of the phytosome, SEM of complex was performed by Scanning Electron Microscope. The powder samples of phytosomes was sprinkled onto the tape.

The aluminum stubs were placed in the vacuum chamber of scanning electron microscope. The sample was observed for morphological characterization using secondary electron detector attached to scanning electron microscopy[12].

Formulation of gels of Phytosome Complex

- Preparation of gel: Gel bases were prepared by separately dispersing Carbopol 934 in distilled water with constant stirring at a moderate speed using mechanical shaker.The pH of all the formulations was adjusted to 5.5 - 6.5 using triethanolamine
- Incorporation of Phytosomal complex into the gel: The solution of phytosome complex was prepared in 0.1 ml of ethanol in another beaker and was added to the Carbopol base. Different formulations were prepared using varying concentration of gelling agent. Prepared gels were stored in suitable containers at room temperature for further studies.

EVALUATION OF GELS OF PHYTOSOME COMPLEX

1. Homogeneity

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container .They were tested for their appearance and presence of any aggregates[11].

2. Measurement of pH

The pH of the phytosome gels were measured with the help of digital pH meter.0.5 g of phytosome gel was dissolved in 50 ml of distilled water and stored for two hrs. The measurementof pH of each formulation was determined[10].

3. Drug content

1 g of the prepared gel was mixed with 100ml of suitable solvent. Aliquots of different concentration were prepared by suitable dilutions after filtering the stock solution and absorbance was measured at 279 nm[10].

4. Rheological study

The measurements of viscosity of prepared gels were carried out with Brookfield Viscometer (pindle type S–96). The readings of each formulation were taken[11].

5. Spreadability

On a glass plate of 10×5cm, 350mg emulgel was taken and another plate of same sized was dropped from a distance of 5cm. After 1 minute the diameter of the circle spread was measured[10].

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CONCLUSION

Numerous investigations and research studies reported antioxidant property of *cassia fistula* and *couropita guianensis* against skin diseases.the objective of the study was to combine them and formulate into phytosome ,an novel drug delivary system which enchances the absorption and bioavailablity of water soluble plant actives. Reflux method employed for the preparation of phytosome using and soya lecithin .the formulation thus made was optimied for maximum entrapment efficiency.the formulated phytosomes was screened for antioxidant activity which concluded tha phytosomes showed antioxidant activity.Thus,the phytosome of the combination of cassia fistula and couroupita guianensis is useful for dermocosmetic applications.

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