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Research article

Rutin phytosomes- For treatment of arthritis

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Abstract

Phytosomes are advanced forms of herbal products that are better absorbed and utilized by the body, and consequently produce better results than conventional herbal extracts. Phytosomes are produced via a patented process whereby the individual components of an herbal extract are bound to phosphatidylcholine—an emulsifying compound derived from soy. Phosphatidylcholine is also one of the chief components of the membranes in our cells. The objective of the present study was to formulate phyto-phospholipid complexes (phytosomes) of Rutin and to evaluate the feasibility for its potential transdermal application in inflammatory conditions for sustained therapeutic benefits. Further Rutin phospholipid complex may be considered as a promising drug delivery system for improving the overall oral absorption and bioavailability of Rutin. . Rutin as colloidal carrier enhanced the drug penetration into the skin, and because of its lipoidal nature, the penetrated drug concentrates in the skin and remains localized for a longer period of time, thus enabling drug targeting to the skin.

Key word- Rutin, artheritis, phytosomes

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1. Introduction

Phytosomes are advanced forms of herbal products that are better absorbed and utilized by the body, and consequently produce better results than conventional herbal extracts. Phytosomes are produced via a patented process whereby the individual components of an herbal extract are bound to phosphatidylcholine— an emulsifying compound derived from soy. Phosphatidylcholine is also one of the chief components of the membranes in our cells.

Application:

The Phytosome process has been applied to many popular herbal extracts, including ginkgo biloba, grapeseed, hawthorn, milk thistle, green tea and ginseng. The flavonoid and terpenoid components of these herbal extracts lend themselves quite well for the direct binding to phosphatidylcholine

2. Materials and methods

Plant profile-

Lemon

Family: Rutaceae Genus: Citrus **Kingdom:** Plantae (unranked): **Angiosperms (unranked):** Eudicots (unranked): Rosids Order: Sapindales Species: C. × Limon **Binomial name Citrus × Limon, often given as C. Limon** (L.) Burm. f.

The flavonoids have strong inherent ability to modify the body's reaction to allergens, viruses and carcinogens. They show anti-allergic, anti-inflammatory, anti-microbial and

anti-cancer activity. Quercetin, myricitin, rutin, tangeritin, naringin and hesperidin are found amongst the common flavonoids in citrus fruits.

Rutin inhibits platelet aggregation, as well as decreases capillary permeability, making the blood thinner and improving circulation. It shows anti-inflammatory activity in some animal and *in vitro* models.

Recent studies show rutin could help prevent blood clots, so could be used to treat patients at risk of heart attacks and strokes. Some evidence also shows rutin can be used to treat hemorrhoids, varicose, and microangiopathy.

Relatively high amount of rutin increases thyroid iodide uptake in rats and decreases serum T3 and T4 level. The decreased hormone level can be explained by its inhibitory effect produced on thyroid peroxides enzyme (TPO). Rutin is also an antioxidant. [5]

Arthritis- Arthritis is a painful and degenerative condition marked by inflammation in the joints that causes stiffness and pain [5, 6].

Arthritis affects the joints and musculoskeletal system. The most common forms of arthritis are osteoarthritis, rheumatoid arthritis infectious arthritis and juvenile rheumatoid arthritis .Most types of arthritis are caused by a combination of factors. These can include genetic makeup, a physically demanding job, previous injury, infection or allergies, certain foods, obesity, autoimmune disease. Physical therapy and occupational therapy can help maintain joint mobility and range of motion. Physical therapy has been shown to delay the need for surgical intervention in advanced cases. Doctors warn that inactivity could harm the health of most patients with arthritis or some kind of rheumatic disease. NSAIDs are the most commonly prescribed drugs for arthritis patients.

Preparation:

Phytosomes were prepared by refluxing followed by solvent evaporation. RN-Ps was prepared in different ratios of Rut into phosphatidylcholine as shown in Table 1. Rutin (RN) was dissolved in methanol in a 200 ml beaker. In a 500 ml round bottomed flux phosphatidylcholine (PC) was dissolved in dichloromethane and Rutin solution was mixed. The mixture was refluxed for 3 hours at 70 °C. After 3 hours the mixture was cooled and then poured to Petridis. The dish was kept open overnight at room temperature for evaporation of solvent. Then the product was kept in hot air oven at 60 °C for 2 hours. The dried product was stored in desiccators for further use [7].

Table 1: Composition of various phytosomes formulations

Ingredients	RN-P (Rutin : Egg lecithin) F1(0.5:1.0)	F2 (0.75:1.00)	F3(1:1)	F4 (1.00:0.75)	F5(1.0:0.5)
Rutin (gm)	0.874	1.312	1.748	2.332	3.497
Egg lecithin (gm)	2	2	2	2	2
Dichloromethane (ml)	80	80	80	80	80
Methanol (ml)	80	80	80	80	80

Parameters studied

Solubility and partitioning

Solubility studies were performed by taking an excess of the sample in 5 ml of various solvent viz. Water, phosphate buffer (pH 6.8), acetate buffer (pH 4.5). Partition coefficient was determined by shake flask method using different solvent systems [8, 9].

Drug entrapment

A weighed quantity of phytosomes equivalent to 10 mg RN was added to 50 ml phosphate buffer pH 6.8 in a 100 ml beaker. The contents were stirred on a magnetic stirrer for

4 hours and then allowed to stand for one hour. Clear liquid was decanted and centrifuged at 5000 rpm for 15 minutes. After centrifugation the supernatant was filtered through 0.45 what man filter paper and after suitable dilution absorbance was measured in UV at 257 nm (UV1800, Shimadju, Japan). The drug entrapment (%) was calculated using the following formula: Drug entrapment (%) = Actual amount determined/Theoretical amount present.

Table 2: Particle size and drug entrapment.

Formulation SD (n=3)	Average particle size (nm)	Drug entrapment (%) (n=3)
Phytosome (0.5:1)(F1)	684 ± 2.44	97.38 ± 1.13
Phytosome (0.75:1)(F2)	780 ± 2.75	95.22 ± 1.33
Phytosome (1:1) (F3)	1202 ± 3.23	99.62 ± 0.93
Phytosome (1:0.75)(F4)	1562 ± 3.45	100.54 ± 1.05
Phytosome (1:0.5) (F5)	1628 ± 3.66	101.08 ± 1.35

3. Results and Discussion

Preparation of phytosomes

We prepared RN-Ps in five different ratios of drug to phosphatidylcholine. All formulations appeared pale yellow color and were in lumps, i.e. not free flowing. Formulations with higher phospholipid content (0.5:1 and 0.75:1) found to be more viscous and sticky lumps. In phyto-phospholipid complex preparation obtaining a clear solution of drug and PC in the reaction solvent is a prerequisite. Dichloromethane was chosen for dissolving PC but rutin is insoluble in this mixture. Rutin is soluble in methanol. Dichloromethane and methanol are miscible with each other at any volume. Rutin and PC were dissolved separately in methanol and dichloromethane respectively and the two solutions were mixed and then refluxed (Table 1).

Solubility-Highest solubility was observed for F3 where the molar ratio of Rutin to Phosphatidylcholine is 1:1. Results show that F3 solubility in phosphate buffer pH 7.4 is much higher (2.025 ± 0.41 mg/ml) than in water (0.774 ± 0.054 mg/ml) and acetate buffer pH 4.5 (0.716 ±0.33 mg/ml). The most satisfactory partition coefficient value for RN-P was exhibited by F3 (3.11 ± 0.08) taking phosphate buffer pH 6.8 as the aqueous medium. Aqueous solubility of drug as well as n-octanol/water partition coefficient are important factors in designing formulations for transdermal application and deciding the fate of per meant for transdermal absorption.

Drug entrapment-All phytosomes formulations contain near to 100 % of drug (Table 3). The results indicate uniform binding of drug and phosphatidylcholine. In formulation F1 and F2 the relatively lower drug content (97.38 % and 95.22 %) may be due to the presence of unbound phosphatidylcholine where Rutin was in 0.5 and 0.75 fraction. In formulation F3, F4, and F5 molar content of RN was higher than phosphatidylcholine and that is why drug and PC obtained sufficient opportunity to interact with each other as PC provide more than one site for drug binding resulting in higher drug content of 99.62 % to 101.08% [11, 12, and 13].

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