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Herbal Bioenhancers Vesicular Drug Delivery System

Swathi GG*

Department of Pharmacology & Toxicology, College of Veterinary Science & Animal Husbandry, China

Corresponding author: Swathi GG

gswa@thi.edu.in

Department of Pharmacology & Toxicology, College of Veterinary Science & Animal Husbandry, China

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Abstract

Numerous issues arise in the field of solubility augmentation. Pharmacosomes, a revolutionary method based on lipid medication delivery, have emerged. Pharmacosomes are covalently bound, colloidal, nanometric-size micelles, vesicles, or hexagonal assemblies of colloidal drug dispersions to the phospholipid. Due to their special qualities such tiny size, amphiphilicity, active drug loading, high entrapment efficiency, and stability, they serve as suitable carriers for drug administration fairly accurately. In addition to lowering therapy costs, drug leakage and toxicity, increasing the bioavailability of poorly soluble medications, and having restorative benefits, they aid in the regulated release of drugs at the site of action. Ayurveda's innovative methods for discovering active ingredients have significantly aided in the discovery of new drugs. A fundamental change in the practise of medicine has been brought about by recent improvements in the bioavailability enhancement of pharmaceuticals by substances of herbal origin. As a outcome, a bibliographic study was conducted by examining traditional textbooks and peer-reviewed articles, accessing internationally renowned scientific databases from the previous 30 years. It has been demonstrated that herbal bioenhancers can improve the bioavailability and bioefficacy of a variety of therapeutic classes, including antibiotics, antituberculosis, antiviral, antifungal, and anticancer medicines, at modest doses. The oral absorption of nutraceuticals such vitamins, minerals, amino acids, and certain herbal components has also been improved. Their primary modes of action involve drug metabolism, drug absorption, and drug target interaction.

Keywords: Antituberculosis; Anticancer

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Introduction

Over the past few decades, the unique drug delivery method has seen extensive use, and emphasis is now being directed to its continued development. Drug delivery at a predetermined rate and for a predetermined amount of time, as well as transporting the active ingredient to the target site, are the two perfect conditions for a system to be considered unique [1]. There is currently no system that can meet all of these requirements. As a outcome, using creative methods to complete them takes a lot of work. These objectives are being met by focusing on drug distribution, either by combining drugs into a carrier system, changing the molecular makeup of drugs, or by restricting drug release in the bioenvironment to determine the distribution profile that has been allocated. One method for increasing drug bioavailability and lowering toxicity by directing the medication to a particular place is the vesicular drug delivery system. Bingham bodies are so named because he discovered the biological genesis of vesicular systems in 1965 [2]. As a outcome, numerous vesicular systems including liposomes, noisomes, and pharmacosomes were developed. There is a decrease in medication toxicity and there are no competing effects because the medicine is delivered directly to the site of action.

The entire process of discovering novel chemical compounds with novel mechanisms of action is the focus of contemporary pharmaceutical research [3]. New drug development technologies have been influenced, in particular, by the economics of therapy related to drug dose. As a outcome, treatments are now more

accessible to a wider range of society members, including those who are struggling financially. Increasing medication bioavailability is one strategy to reduce drug dosage and, consequently, drug toxicity and cost. Man's use of antibiotics and other medications is rising alarmingly quickly [4]. Depending on the type of antibiotic, 20–50% of the total medications and chemicals used are not necessary. Additionally, the indiscriminate use of antibiotics encourages the development of drug resistance to many classes of antibiotics, making it challenging to control disease [5]. The fact that infected people need to take more antibiotics may be related to (1) decreased gut membrane absorption when taken orally, (2) restricted target microbe uptake, and (3) efflux pump activity resulting in indiscriminate antibiotic or therapeutic molecule extrusion. Therefore, the majority of the medicine applied is wasted, and just a small portion is directed toward the infection site. Additionally, the quantity of unutilized drugs and antibiotics builds up in the body and environment as a load, functioning as a selection pressure that promotes the development of drug resistance and, ultimately, outcomes in the failure of antibiotics to treat resistant illnesses [6]. In addition, this is the cause of the negative impacts, illnesses, and shortened life span.

The issue of selection pressure and drug toxicity will persist if two medications are taken at the same time that has antibacterial properties. The demand for molecules known as bioenhancers-molecules that improve the effectiveness and availability of primary medications in combination therapy-instead of antibacterial or target medicines [7]. Due to the fact that these chemicals do not cause any selection pressure for mutants to become resistant to them, their negative effects can be reduced. The process of resistance developing will be markedly slowed down, ultimately extending the shelf life of both new and old antibiotics. Such medications/molecule facilitators should have cutting-edge qualities including being (1) harmless to people or animals, (2) efficacious at very low concentrations in combination, and (3) simple to use.

An agent of herbal origin or any phytomolecule that has the ability to increase the bioavailability and bioefficacy of a certain medicine or nutrient with which it is coupled is known as a herbal bioenhancers [8]. At the dose used, this agent has no normal pharmacological activity of its own. An improved antiasthmatic effect of an Ayurvedic formula including vasaka (Adhatoda vasica) when administered with long pepper was noted by Bose, a renowned author of "Pharmacographia Indica," in the 1920s. Indian scientists first used the term "bioavailability enhancer" in 1979 when they identified piperine as the first bioavailability enhancer in the world and scientifically confirmed it at the Regional Research Laboratory in Jammu (RRL, now known as Indian Institute of Integrative Medicine).

Pharmacosomes

A neutral molecule having a balanced ratio of polyphenol to phospholipids in a complex form, a love of both water and fat, and a positive and negative charge may be referred to as a pharmacosome. In these lipoidal drug delivery systems, the medicines are dispersed and coupled to lipids either through hydrogen bonds with lipids or by electron pair sharing and electrostatic interactions. From the Greek words "pharmakon" for drug and "soma" for carrier, the word "pharmacosome" is derived. It refers to a system of vesicles where the medicine and the carrier are linked. Depending on the structure of the complex, these lipid conjugated vesicles can be hexagonal assemblies with a functional hydrogen atom or colloidal, nanometric-sized micelles.

(A) The conjugate's physical and chemical characteristics regulate the stability of the entire system.

(b) Because they possess both water- and fat-loving qualities, they can easily pass through cell membranes, cell walls, or tissues when exocytosed or endocytosed, respectively.

(c) The size of the drug molecule, the type of functional group it contains, the length of the fatty acid chain in lipids, and the presence or absence of a spacer all affect how quickly it degrades. To achieve the best in vivo pharmacokinetic behaviour, all of these variables can be changed.

(d) They may be delivered orally, topically, extravasally, or intravenously.

Ether-Injection Technique

This method involves dissolving the drug-lipid combination in an organic solvent. Vesicles are created when this mixture is gently injected into an aqueous agent that has been heated. The concentration affects the condition of amphiphiles. Amphiphiles introduce a monomer state while the concentration is lower, but as the concentration raises, several types of structures, such as spheres, cylinders, discs, cubic crystals, and hexagons, may emerge. Prodrug of Diglyceride and a common surfactant, dodecylamine hydrochloride, were compared for their effects on interfacial tension by Mantelli and colleagues. It was determined that the prodrug displayed a liquid-crystalline phase, exhibiting massive molecular structures, above the critical micellar concentration, when long cylinders were seen arranged hexagonally.

Stability of Pharmacosomes

The stability of the system is assessed by comparing the spectrum of a complex at different periods in time in the solid state with the spectrum of dispersion in water composed of tiny particles.

Solubility

Shake-flask technique can be used to assess the change in solubility brought on by complexation. In this method, the organic phase, 1-octanol, and the aqueous phase, buffer solution with proper pH and drug-phospholipid conjugate, are combined. After continuous shaking, equilibrium is maintained at 37°C for one day. After the aqueous phase has been separated, either UV or HPLC method is used to determine the concentration.

Drug-Lipid Compatibility

Drug-lipid compatibility and potential interactions are assessed using the thermo analytical method known as differential scanning calorimetry. Using various samples heated in a closed

sample pan, the thermal response is investigated. The nitrogen gas is expelled, and a predetermined range of temperature is maintained with a predetermined heating rate.

Herbal Bioenhancers

The primary plant alkaloid found in P. nigrum Linn (black pepper) and P. longum Linn (long pepper) increases the bioavailability of various foods and medications. It has been frequently employed as a savoury food condiment and flavouring. Various ailments, including seizure disorders, have been treated using piper species in folkloric medicine. Piperine is known to exhibit a wide range of biological activities, including anti-inflammatory, antipyretic, fertility-improving, antifungal, antidiarrheal, antioxidant, antimetastatic, antithyroid, antimutagenic, antitumor, antidepressant, antiplatelet, analgesic, hepatoprotective, antihypertensive, and antiasthmatic activity.

Naringin and Paclitaxel

Rats were used in the study to determine how oral naringin affected the pharmacokinetics of intravenous paclitaxel. Prior to the intravenous (3 mg/kg) dose of paclitaxel, oral naringin (3.3 and 10 mg/kg) was pretreated for 30 minutes. When paclitaxel was administered intravenously, the AUC was significantly higher (40.8% and 49.1% for naringin dosages of 3.3 and 10 mg/kg, respectively) and decreased noticeably more slowly (29.0% and 33.0%, respectively) than in controls. The much higher AUC may be mostly attributable to oral naringin's suppression of paclitaxel's CYP3A1/2 metabolism. The much higher AUC of intravenous paclitaxel by oral naringin may potentially be attributable to the drug's suppression of hepatic P-glycoprotein.

Cow Urine Distillate

Cow urine alone is not as effective as cow urine distillate as a bioenhancer to boost the potency of antifungal, antibacterial, and anticancer medications. Cow urine can be utilised as a bioenhancer of zinc and has antitoxic properties against the toxicity of cadmium chloride. Cadmium chloride exposure reduced the reproductive rate of mature male mice to zero percent. Animals exposed to cadmium chloride, cow urine distillate, and zinc sulphate, on the other hand, displayed a 90% reproductive rate, 100% viability, and 100% lactation indices. The fertility index in the group receiving cadmium chloride plus cow urine distillate was likewise determined to be 88%. These findings show that cow urine distillate is a bioenhancer of zinc and acts as an antitoxic against the toxicity of cadmium chloride. Gonadotropin-releasing hormone conjugate was improved by cow urine distillate on the reproductive hormones and estrous cycle of female mice. The effect of gonadotropin-releasing hormone on the gonadosomatic indices, sperm motility, sperm count, and sperm morphology was considerably improved by cow urine distillate, notably in the 90- and 120-day treatment groups (0.05p) in male mice. Due to its immunomodulatory qualities, cow urine distillate amplified these effects.

Stevia rebaudiana

Stevia rebaudiana, sometimes known as honey leaf, has been a popular sweetener in South America for many years. Stevioside, a glycoside that is 200 times sweeter than sucrose, makes up the majority of the stevia plant. The following substances are also present: steviol, austroinulin, rebaudioside, and dulcoside A. Selectively increasing the bioavailability/bioefficacy of medications, nutraceuticals, and herbal drugs/formulations is possible with extracts/fractions/pure isolates of stevia either alone or in conjunction with piperine. From 0.01 to 80% of the bio-enhancement mix contains stevia. The dosage for piperine is between 0.01 and 12 mg per kilogramme of body weight, whereas the dosage for bioenhancer generated from stevia extract is between 0.01 and 50 mg per kilogramme.

Allicin and Cu^{2+}

Cu^{2+} exhibited dose-dependent fungicidal activity against Saccharomyces cerevisiae cells, and the addition of allicin, an allyl sulphur molecule found in garlic, greatly increased the fatal effect of Cu^{2+}. Other sulfur-containing substances like N-acetyl-cysteine, l-cysteine, or dithiothreitol had no effect on or rather decreased the fungicidal activity of Cu^{2+}. In contrast to the fungicidal activity of newly produced Cu^{2+} in combination with allicin, Ca^{2+} demonstrated no protection against the deadly effect of Cu^{2+} alone. Cu^{2+} increased the production of endogenous reactive oxygen species (ROS) in S. cerevisiae cells to a lethal level, although this intracellular elevation of oxidative stress was not seen as the cell death process progressed after treatment with Cu^{2+} plus allicin. Sodium N-lauroyl sarcosinate is a surfactant (SLS).

Discussion

By using stoichiometric ratios of lipid and herbal ingredient in a specific solvent, phytosomes are a combination of an herbal medication and lipids like soy lecithin. The interaction of the polar functional groups of the substrate and phosphate as well as the ammonium groups of the polar head of the phospholipid by creating hydrogen bonds was explained by spectroscopic analysis. In this instance, the phospholipid polar head is used to anchor the phytoconstituent. As an outcome, it combines with the membrane. For instance, a hydrogen bond is formed between the phosphate group of phosphatidylcholine and the hydroxyl group in the phenols of the flavone moiety in the phosphatidylcholine and catechin combination. When the complex's nuclear magnetic investigations were carried out and contrasted with those of its pure ancestors. By increasing drug absorption to the digestive tract in comparison to unbound phytoconstituents and establishing a stable complex with phospholipids, phytosomes enhance the bioavailability and stability profiles.

Due to their increased solubility in bile salts, phytosomes can be employed to target the liver.Because active phytoconstituents are more effectively absorbed, the dosage of the medicine is decreased. In addition to serving as a carrier, PC has a synergistic hepatoprotective impact with phytosomes. Phytosomes' enhanced skin penetration and high lipid profile make them suitable for usage in the cosmetics sector.

Conclusion

In the pharmaceutical industry, vesicular systems are a new type

of carrier system. They nonetheless function as a crucial tool for medication targeting and sustained release despite having drawbacks such as being fused and aggregated. Additional drug destiny and biological activity may be changed with the enhancement of spacer groups and connections. The investigation of nonbilayer phases and the study of the mechanism of action, however, still call for further efforts. Therefore, pharmacosomes have enormous promise for enhancing drug delivery for both natural and artificial active ingredients. Current research trends include cellular targeting utilising various techniques like PEGylation, biotinylation, and so on. To increase dietary components' in vivo performance and eventually maximise their efficacy as a bioavailability enhancer, an efficient formulation method for the adjustment of the pharmacokinetic features of dietary components is essential. According to the available scientific studies, coadministering or pretreating bioenhancers with various medications and nutraceuticals outcomes in a significant enhancement of their bioavailability. This list of organic substances also includes piperine, Zingiber officinale, niaziridin, glycyrrhizin, Cuminum cyminum, Carum carvi, allicin, lysergol, Aloe vera, Stevia rebaudiana, curcumin, sinomenine, genistein, Ammannia multiflora, capsaicin, quercetin, naring As a outcome, medication resistance, drug toxicity, and adverse drug reactions are decreased by lowering the dose and shortening the course of treatment. Treatment is cost-effective because of dose economy. Bioenhancers are also discovered to have a decreased effect, no effect, or minimal impact on the bioavailbility on some drugs.

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Conflict of Interest

The author has no known conflict of interest associated with this paper.

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