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EVALUATION OF THE EFFECTIVENESS OF USING LIPOSOMAL FORMS OF VITAMINS, USING VITAMIN C AS THE EXAMPLE

E. R. Tukhvatulina, M. J. Baltaeva

Tashkent Pediatric Medical Institute

Annotation. Vitamin C is an exogenous compound required for various metabolic processes; therefore, effective delivery is critical to maintaining body homeostasis. The pharmacokinetics of vitamin C and its low amounts in processed foods require its continuous supplementation. In this article, we present a review of a new liposomal vitamin C formulation free of harmful organic solvents. The formulation was quantitatively characterized in terms of its chemical composition and nanostructuring. Encapsulation of vitamins and minerals in liposomes helps improve overall bioavailability.

Key words: Liposome, pharmacokinetics, bioavailability

Аннотация. Витамин С является экзогенным соединением, необходимым для различных метаболических процессов; поэтому эффективная доставка имеет решающее значение для поддержания гомеостаза организма. Фармакокинетика витамина С и его низкие количества в обработанных пищевых продуктах требуют его постоянного добавления. В статье мы представляем обзор на новую липосомальную формулу витамина С, свободную от вредных органических растворителей. Формула была количественно охарактеризована с точки зрения ее химического состава и наноструктурирования. Инкапсуляция витаминов и минералов в липосомы помогает улучшить общую биодоступность.

Ключевые слова: Липосома, фармакокинетика,биодоступность.

Annotatsiya. S vitamini turli metabolik jarayonlar uchun zarur bo'lgan ekzogen birikma; shuning uchun samarali etkazib berish tananing gomeostazini saqlab qolish uchun juda muhimdir. S vitaminining farmakokinetikasi va qayta ishlangan oziq-ovqatlardagi past darajalari uni muntazam ravishda qo'shishni talab qiladi. Ushbu maqolada biz zararli organik erituvchilardan xoli C vitaminining yangi liposomal formulasini ko'rib chiqamiz. Formula kimyoviy tarkibi va nanostrukturasi bo'yicha miqdoriy jihatdan tavsiflangan. Liposomalardagi vitaminlar va minerallarni kapsulalash umumiy bioavailabilityni yaxshilashga yordam beradi.

Kalit so'zlar: lipozoma, farmakokinetika.

Today, the creation of new groups of drugs with improved pharmacokinetic properties is an important area of modern medicine. One of the areas of modern pharmacology is the method of drug delivery and their bioavailability. This article provides an overview of

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vitamin C in liposomal form, its delivery to organs and tissues, as well as possible side risks of using this form of vitamin.

Vitamin C is an important antioxidant, it protects organs and tissues from damage caused by free radicals by activating the body's defenses, enhances and accelerates the repair of wounds and scars. Vitamin C is a vital vitamin because it participates in the synthesis of hyaluronic acid, collagen and elastin, is a cofactor of minerals such as calcium, zinc, and also affects the synthesis of cholesterol. Vitamin C accelerates protein and carbohydrate metabolism. It is a powerful detoxifier, accelerating the removal of toxic substances from the body: lead, copper, mercury, vanadium. Vitamin C participates in detoxification processes in hepatocytes with the participation of cytochrome P 450. The vitamin participates in the synthesis of interferon, having a direct effect on immunomodulation processes. Vitamin C is also a cofactor in iron absorption, improving the absorption of iron from food by converting the Fe3+ ion to Fe2+ with the formation of a complex compound.

Research is currently underway to determine the neuroprotective effects of ascorbic acid in Alzheimer's disease and the prevention of age-related cognitive decline. However, avoiding vitamin deficiency appears to have a more beneficial effect than taking large doses as supplements to a healthy diet. Vitamin C plays an important role in strengthening blood vessels, increasing the body's endurance, enhancing exercise tolerance. In plasma, it increases endothelium-dependent vasodilation and reduces extracellular oxidants from neutrophils. Vitamin C deficiency leads to the potentially fatal disease scurvy, a low immunity that can only be cured by taking the correct dose of vitamin C. Vitamin C is not synthesized or accumulated in the body, so it must be replenished regularly. Conventional forms of ascorbic acid are not fully absorbed, are quickly destroyed, and irritate the gastrointestinal mucosa. The main advantages of vitamin C enclosed in a liposomal shell are high bioavailability and protection of the digestive tract mucosa from irritation even when taking high doses. The liposomal shell consists of phospholipids, which serve as additional building material for damaged cell membranes.

Vitamin C contained in food or dietary supplements is broken down in the stomach. But the highly acidic environment of hydrochloric acid can partially neutralize it. To help vitamin C survive in an acidic environment, its water-soluble molecule is encapsulated in a liposome. This fat capsule forms a protective shield around vitamin C, protecting it from acid and transporting it to the small intestine for further absorption. Since most fat digestion occurs in the small intestine, vitamin C is released there after enzymes from the gallbladder and pancreas help break down lipids. Liposomes are vesicles that simply mimic the highly complex cell membranes comprising lipid bilayers surrounding an aqueous core, which have attracted considerable attention for the delivery and protection of both hydrophilic and hydrophobic compounds such as vitamins due to their unique properties of biocompatibility and biodegradability. Accordingly, liposomes can promote the protection and activity of vitamin C.

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Only a few studies have been published showing the effect of liposomal encapsulation on the bioavailability of vitamin C. Hickey et al. (Citation2008) found in a very small study involving only two subjects that the bioavailability of liposomal vitamin C was no different from that of a 5 gram vitamin C tablet. However, in liposomal vitamin C consisting of higher dosages such as 20 and 36 g, plasma vitamin C levels resulted in higher plasma levels than ever previously shown in the literature. This result indicates that liposomes may be an excellent carrier of vitamin C to achieve higher blood levels of vitamin C that cannot be achieved with other dosage forms. Davis et al. (Citation2016) assessed plasma levels of oral, intravenous, and oral liposomal vitamin C. The results showed that liposomal vitamin C has increased bioavailability than non-liposomal vitamin C while avoiding the risks associated with intravenous administration (Davis et al. Citation2016). However, no real-world bioavailability studies have been published for the absorption of liposomal vitamin C (Davis et al. Citation2016). In 2019, a single-blind study was conducted that measured plasma vitamin C levels in two subjects in samples taken every half hour or every hour for 6 hours after vitamin C ingestion. The data were compared with published results and with 10 years of laboratory plasma determinations. Subjects took 1 gram vitamin C tablets; liposomal vitamin C. Plasma levels were analyzed using the Butts and Mulvihill method. Preliminary studies of the effects of liposomal and standard ascorbate have concluded that repeated doses can maintain levels well above the previously estimated maximum. These findings have implications for the use of ascorbate as a nutrient and as a drug. With frequent oral administration, equivalent plasma levels can be maintained indefinitely. Thus, oral vitamin C has the potential to be used as a non-toxic, sustainable therapeutic agent. A 2021 study was conducted with the primary objective of evaluating the comparative kinetics of vitamin C accumulation in leukocytes over 32 hours following acute administration of 250 mg or 500 mg from the two sources. Secondary objectives were to evaluate neutrophil phagocytic function and lymphocyte differentiation between the two vitamin C sources. Ninety-three healthy women (250 mg, n = 27; 500 mg, n = 24) and men (250 mg, n = 19; 500 mg, n = 23) were assigned to receive a single dose of CA or AA providing 250 mg or 500 mg vitamin C in two separate, double-blind, randomized, crossover trials. Study results revealed no significant differences in the primary or secondary outcomes between the two treatments in the low-dose 250 mg trial. In contrast, there was evidence that 500 mg CA increased plasma docosahexaenoic acid levels, increasing neutrophil functionality during the first 8 hours of the study. These results suggest that 500 mg CA may provide some immune benefits compared to 500 mg AA.

A review of the literature has shown that vitamin C may have beneficial effects on blood pressure, infections, bronchospasm, atrial fibrillation, and acute kidney injury. However, the practical significance of these effects is unclear. A review of meta-analysis data assessed the effect of vitamin C on the practical outcomes of intensive care unit (ICU) length of stay and duration of mechanical ventilation. Eighteen controlled trials with a total of 2004 patients were analyzed, 13 of which studied patients undergoing elective heart surgery. The analysis of the data showed that in 12 trials with 1766 patients, vitamin C reduced the length of ICU

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stay by an average of 7.8%. In six trials, oral liposomal vitamin C at doses of 1-3 g/day (weighted mean 2.0 g/day) reduced the length of ICU stay by 8.6%. The effect of vitamin C on ICU patients should be studied in more detail. In conclusion, it should be noted that the inability to produce endogenous vitamin C and uncertain dietary intake can lead to a deficiency that can be easily corrected by effective supplementation. Most of the vitamin C in the human body is found intracellularly (over 97%), while only a small portion is found in extracellular fluids. A complex system of ascorbic acid fluxes in the human body prevents excessive fluctuations in its intracellular concentrations, as required by metabolic processes. In order to influence the homeostatic balance using a convenient oral route of delivery, vitamin C intake must be high enough and preferably spread out over time. To achieve this, high concentrations of vitamin C in the gastrointestinal tract must be maintained for a long time so that it is available for absorption and does not require repeated dosing. Maintaining high levels of vitamin C in the gastrointestinal tract depends mainly on the rate of its hydrolysis. The degradation of vitamin C can be significantly reduced by its association with lipid interfaces, which are abundant in the liposomal formulation. This means that if a certain concentration of ascorbic acid in the digestive tract is maintained for a sufficient period of time, a high level of absorption will be achieved and maintained. Another important aspect of the liposomal formulation is the ability to deliver large doses of vitamin C over a long period of time, since the lipid capsule alleviates the gastrointestinal irritation that usually accompanies large oral doses of ascorbate. Another important feature of the presented formula is that the process of liposome formation does not require toxic organic solvents.

In summary, encapsulation of vitamin C in novel types of liposomes results in enhanced bioavailability of vitamin C at physiological level without compromising its efficacy at cellular level. Liposomal vitamin C formulation, in addition to its high activity provided by enhanced bioavailability, should also satisfy stringent regulatory requirements regarding the content of potentially harmful compounds, stability and reproducibility of manufacturing processes. Liposomally encapsulated ascorbic acid (vitamin C) exhibits well-organized morphological structure, uniform particle size and high efficiency, resulting in enhanced bioavailability. The structural formation of liposomes makes them a versatile nanocarrier with the capabilities of loading and delivering multiple drugs/components for specific disease states. Furthermore, with the advent of combination drug therapy and the development of new drug products using liposomal formulations, which have shown significant advantages over traditional drug therapies, there is great potential in this class of drugs, which can be considered as a preferred drug delivery strategy.

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