

Formulating A Highly Bio Available Water Soluble Full Spectrum Nano Cannabinoids with Botanical Bio Potentiators- A Nano Emulsion Technology

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For a long time herbal medicines were not considered for development as novel formulations owing to lack of scientific justification and processing difficulties, such as standardization, extraction and identification of individual drug components in complex polyherbal systems. However, modern phytopharmaceutical research can solve the scientific needs (such as determination of pharmacokinetics, mechanism of action, site of action, accurate dose required etc.) of herbal medicines to be incorporated in novel drug delivery system, such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles and so on.

Drug delivery technology market offers a promising approach for the delivery of drugs through various routes of administration. Drug delivery technology is aimed at maximizing the drug delivery at the targeted site so as to increase the efficiency of drug and proposing improved patient compliance.

The major factors responsible for the growth of the drug delivery technology market are the rising prevalence of chronic diseases, growth of the biologics market, new product launches, and innovation and technological advancements. Owing to these factors, the demand for drug delivery technologies such as metered dose inhalers, dry powder inhalers, soft mist nebulizers, topical gels and trans dermal patches, self-injection devices, and wearable injector are increasing. On the other hand, regulatory hurdles and pricing pressure, patent expiry and patent cliff, product recall, and increase injuries and side effects are expected to restrain the growth of this market.

Administration of active phytochemical components into the human body requires the use of an appropriate vehicle for bringing an effective pharmacological effect of the active component to be transported to the target site in the body. The desired site varies and it may be the blood stream, organs and cells, and so on. Majority of phytochemicals, such as phyto cannabinoids, are either poorly soluble as all natural cannabinoids are highly lipid soluble.

It is known that the delivery of these phyto cannabinoids is significantly influenced by their physicochemical properties, such as water solubility, partition coefficient, lipophilicity and crystallinity, and so on. A major obstacle in the development of cannabinoid based drug has been the lower water solubility which makes it difficult to develop effective formulation for human use.

Nanoemulsion

Constructing an appropriate vehicle and the desired efficient formulation possess a challenge to the medical cannabis industry. To overcome the instability, poor water solubility, and to enhance the bioavailability of these phyto cannabinoids one option is to entrap these phyto cannabinoids into a matrix of nanoemulsion. Nano emulsion based delivery system have been proved to be one of the best platform to enhance the bio availability and biological effectiveness of different phytochemicals.

Nanoemulsions have been successfully used for many years in the food, cosmetic, pharmaceutical and chemical industries. Nano emulsions has the potential to greatly increases the bioavailability of cannabis based products such as tablets, capsules, creams and sprays.

Nanoemulsions are a class of extremely small droplet emulsions that appear to be transparent or translucent with typical colour. They contain continuous phase, dispersed phase and emulsion stabilizer, the emulsifier or called the surfactant. They are usually in the range 50 to 200 nm.

Compared with conventional methods, such as co-solvent addition, micronizing/milling, spray drying and salt formation, the use of lipid based delivery systems, such as micro/nanoemulsions and micelles, offer many advantages like (i) high kinetic or thermodynamic stability, which provides significantly better stability over unstable dispersions. (ii) either hydrophilic or lipophilic phytochemicals can be incorporated into the same nanoemulsions; and

(iii) because of the small droplet sizes, phyto cannabinoids can be transported through the cell membranes much more easily, resulting in an increased phyto cannabinoid concentration in plasma and bioavailability.

Cannabis extracts are mostly lipophilic (hydrophobic), and hence to have a proper absorption in the human system, it is to be made into water soluble nanoemulsion with a water dispersion stabilized by an interfacial film of surfactant molecule having droplet size range 20–600 nm.

As cannabis being a Schedule 1 drug, there has been little tests done on the bio availability. Though few tests were done on animals, it is not translating the same results in human.

It is been reported that, the oral bio availability of cannabinoids range from 13-19% and inhalation bioavailability is between 11-45% (mean 31%). So to have higher bio availability, it is better to be formulated into a highly bio available compound using bio availability enhancers.

Biopotiation or bioavailability enhancing

“The phenomenon of increasing the total availability of any chemical entity (nutrient or drug molecule) in biological fluid or systemic circulation is called biopotiation or bioenhancement and the secondary agents which are responsible for this augmentation of plasma concentration of principle ingredient are termed as Biopotentiators or Bioavailability enhancers”.

Advantage of bioenhancement

Bioavailability is directly proportional to the available plasma concentration so ultimately related therapeutic efficacy.

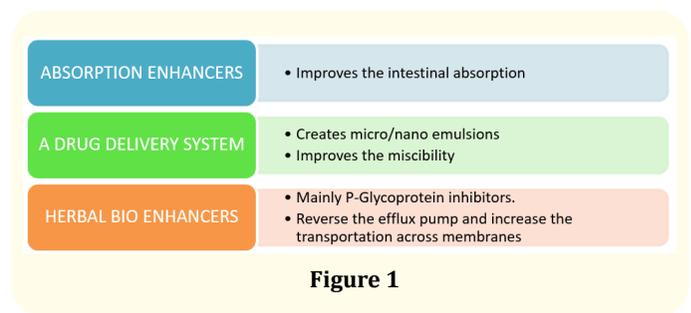
1. This can make the expensive drugs affordable by lowering the dose or dosing frequency. Shortening the treatment period also increase the acceptance of patients mainly in case of chemotherapy. It comforts the patient in terms of cost also.
2. Reduce the required dose ultimately reduce the toxic effects.
3. Therapeutic treatments which include heavy doses, accompanied by loss of metals and vitamins available in body. The bioenhancers improve the nutritional status of body while duration of course.

While developing a drug delivery system for a cannabis based product, the knowledge on the cannabinoids receptor site is important to select the ingredients. Because of their lipophilic character, cannabinoids can penetrate cellular membranes by diffusion. The

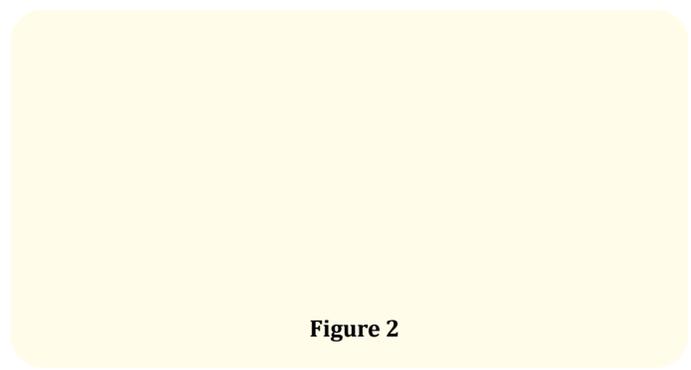
possible explanations for cannabinoid activity included unspecific membrane binding resulting in fluidity- and permeability changes of neural membranes, the inhibition of acetylcholine-synthesis, an increase in the synthesis of catecholamines, and an interaction with the synaptosomal uptake of serotonin. However, it was established in the mid 1980s that cannabinoid activity is highly stereo selective indicating the existence of a receptor mediated mechanism. The human cannabinoid receptors are of two types. CB1 receptors, which are present mainly in brain and spinal cord. CB2 receptors, present in spleen and immune cells. Both are 7 helix transmembrane receptors coupled to G-Protein.

While selecting the ingredients care must be taken that these inert ingredients should not be toxic to human, should not alter the molecular structure of active ingredients and have to enhance the storage stability. Also, the ingredient must be listed in FDA regulations.

Based on the science, we select the key inert ingredients, which have the following pharmacological activity.



Cannabi-na™ is a water soluble nano cannabinoid, that can be used in the formulation of oral, pulmonary, dermal and nasal routes. It can also be used in the formulation of health drinks, candies and chocolates.



The advantages of using Cannabi-na™ is as below (Figure 3).

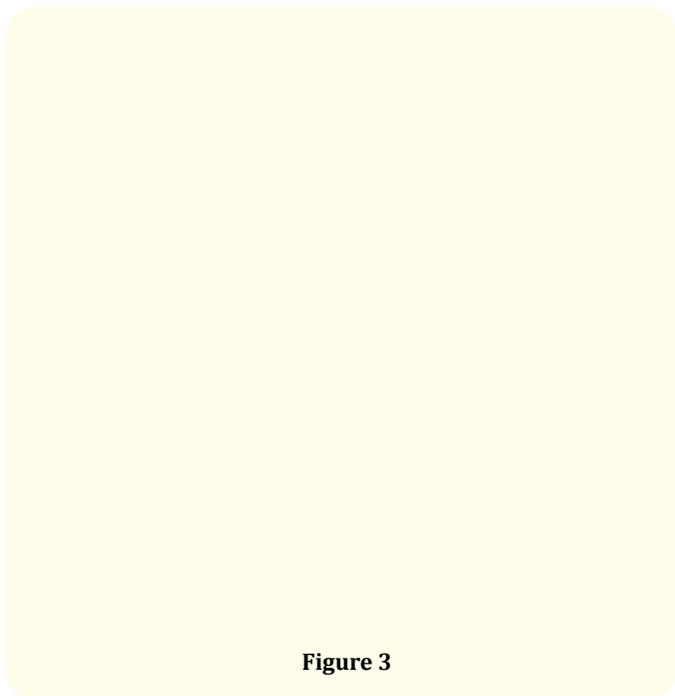


Figure 3

The manufacturing system of Cannabi-na™ comprises of 3 reactors. Each reactor receives proprietary ingredients, which convert the crude cannabinoids or pure fractions of cannabinoids into a water soluble compound. The attached PFD explains the process in detail.

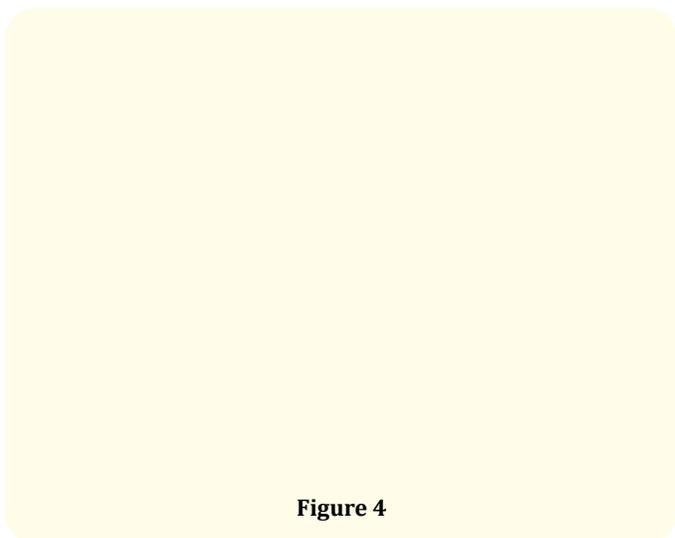


Figure 4

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