NanoSphere Delivered CURCUMIN

When a nutraceutical is given orally, its bioavailability and, ultimately, its efficacy depend on the solubility and absorption in the gastrointestinal tract. Curcuminoids (hereafter Curcumin) have a very low bioavailability and efficacy when taken orally due to several interacting reasons. Curcumin is comprised of hydrophobic molecules that are practically insoluble in aqueous solutions. Due to this water-adverse nature, Curcumin has poor oral absorption due to slow or incomplete dissolution in the lumen of the gastro-intestinal tract. Furthermore, Curcumin undergoes rapid glucuronidation (chemical binding to glucuronic acid) upon oral administration that keeps plasma levels low despite a high intake of Curcumin. Also, the water-adverse nature of Curcumin inhibits entry into cells and desired targets.

Increasing the Bioavailability of Curcumin

The solution for increasing the oral bioavailability and efficacy of Curcumin is to formulate Curcumin into a ‘NanoSphere’ delivery system that 1) improves the absorption of Curcumin from the gut into the systemic circulation, 2) shields the molecules of Curcumin from extensive pre-systemic metabolism, 3) avoid uptake by the Reticuloendothelial System and 4) transports Curcumin into the cells of desired targets. A solid lipid NanoSphere delivery can accomplish these actions.

Curcumin is a lipid-soluble molecule with a preferential attraction to lipid membranes. Thus, its entrapment and complex-formation into phosphatidylcholine lipid NanoSpheres (ie solid lipid nanoparticles or related encapsulated delivery systems) are recognized as a way to achieve highly effective delivery vehicles for a wide range of biological activity.

Solid Lipid NanoSpheres formed from purified-soya phosphatidylcholine, phospholipids and fatty acids can readily entrap Curcumin, efficiently transporting Curcumin across the gastro-intestinal barrier, while protecting Curcumin from decomposition by the enzymes present in the gastro-intestinal environment. Furthermore Curcumin NanoSpheres appear to shield Curcumin from metabolic changes which substantially raise plasma levels of Curcumin for a longer period of time. NanoSpheres appear to mblock the rapid glucuronidation upon oral administration that keep plasma Curcumin levels low despite a high intake of Curcumin.

Research confirms that NanoSpheres vesicles containing Curcumin may be the most efficient means today for delivering curcumin into the circulatory system cells and targets throughout the body.

- In a rodent study, nano-encapsulated Curcumin—formulated with phosphatidylcholine-enriched soybean lecithin—achieved peak plasma levels and area under the plasma concentration time curve (AUC) values that were five-fold higher than the equivalent values seen after unformulated Curcumin. Similarly, liver levels of Curcumin were higher after administration of formulated Curcumin as compared to unformulated Curcumin.

- Plasma levels of curcumin sulfate, curcumin glucuronide, tetrahydrocurcumin, and hexahydrocurcumin observed after administration of nano-encapsulated curcumin were 3- to 20-fold higher than those seen after non-encapsulated Curcumin.
• Nano-encapsulated Curcumin formulating with phosphatidylcholine produce significantly higher systemic levels of Curcumin than non-encapsulated Curcumin. They can maintain an effective concentration of Curcumin in the serum for a longer period of time.

• Curcumin-biodegradable NanoSpheres could be successfully employed as a prolonged-release delivery system for better therapeutics. Curcumin NanoSpheres have exhibited a typical biphasic release pattern characterized by a typical burst-effect followed by a slow release that may continue for several days.

Traditionally, turmeric has been used for many ailments, particularly as an anti-inflammatory agent, and curcumin has been identified as the active principle of turmeric. Curcumin has been shown to exhibit antioxidant, anti-inflammatory, antimicrobial, and anticarcinogenic activities. Additionally, the hepato- and nephro-protective [liver- and kidney-protective], thrombosis-suppressing, myocardial infarction-protective, hypoglycemic, and antirheumatic effects of curcumin are also well established. Various animal models or human studies proved that curcumin is extremely safe even at very high doses. . . Similarly, the efficacy of curcumin in various diseases, including cancer, has been well established. Several clinical studies dealing with the efficacy of curcumin in humans can also be cited. The pharmacological safety and efficacy of curcumin makes it a potential compound for treatment and prevention of a wide variety of human diseases.

Enhanced Antioxidant and Hepatoprotection

The greater bioavailability and bioactivity from encapsulating Curcumin into Lipid NanoSpheres may increase the potential scope of biomedical and nutraceutical applications for Curcumin. Nano-encapsulated Curcumin-phospholipid complexes have demonstrated significantly greater antioxidant activity hepatoprotective actions than free Curcumin at the same dose level due to better absorption and bioavailability. They have significantly protected the liver by restoring the enzyme levels of the liver glutathione system and that of superoxide dismutase, catalase, and thiobarbituric acid reactive substances

Curcumin bound to phosphatidylcholine micelles is a potent inhibitor of lipoxygenase-catalyzed fatty acid peroxidation of linoleic acid and arachidonic acid due to binding the active center iron. Arachidonic acid lipoxygenases are involved in the pathogenesis of various diseases, such as allergy, atherosclerosis, and cancer.

Better Blood Brain Penetration and Neuroprotection

The low-molecular weight structure of Curcumin NanoSpheres may increase the amount of Curcumin that can cross the blood-brain barrier, past the protective cell membranes of neurons and into neurological structures targets for greater neuroprotection. This can improves Curcumin’s actions that oppose Alzheimer’s and Parkinsonism. Curcumin has demonstrated the ability to inhibit the formation of amyloid β oligomers and fibrils, reduce plaques, and reduce amyloid. Orally administered Curcumin reduces central nervous system inducible nitric-oxide synthase, inflammatory cytokines, and lipid peroxidation.
Curcumin may be beneficial in inhibiting the development of retinopathy in diabetic patients. However, unformulated Curcumin has poor oral bioavailability limiting its potential in the retina. Encapsulating Curcumin in lecithin NanoSpheres may provide higher concentrations to inhibit diabetic retinopathy.

**Cancer Prevention**

The role of Curcumin for the treatment of cancer has been an area of growing interest. Curcumin in its free form is poorly absorbed in the gastrointestinal tract and limited in its clinical efficacy. Lecithin-based NanoSphere encapsulations of Curcumin can circumvent the problem of poor oral availability that limits the utility of free Curcumin and allow for allow systemic administration.

The activity of a lipid-Nanosphere encapsulated Curcumin was equal to, or better than, free Curcumin at equimolar concentrations in down-regulating the NF-β machinery, suppressing growth, and inducing apoptosis of human pancreatic cells. In vivo, a lecithin microsphere of encapsulated Curcumin inhibits pancreatic cell growth and these effects are accompanied by a potent anti-angiogenic response. And lipid microspheres of encapsulated Curcumin have anti-tumor and anti-angiogenesis effects against colorectal cancer in vitro and in vivo.

**Curcumin C3 Complex - The Preferred Curcumin Extract**

Curcumin is a polyphenolic compound, and the principal active ingredient in turmeric; it shares its therapeutic role with two closely related compounds called curcuminoids: demethoxycurcumin and bis(demethoxy)curcumin. In the context of medicine or nutrition, either of the terms curcumin or curcuminoids is usually understood to mean all three of these compounds, which appear to act in concert. A preferred commercial curcumin extracted from turmeric known as Curcumin C3 Complex contains high amount of these three compounds in an optimal ratio.

The Curcumin C3 Complex has been clinically tested and is certified by NSF International for potency and specification compliance. This Curcumin Complex extract is patented and has been used for a wide range of research that include colorectal cancer, immunological mechanism in Alzheimer’s disease, alcoholic hepatitis, free radical quenching, anti-inflammatory activities, and anti-cancer potentials.

Below are a few examples of the types of research activities and institutions where C3 Complex is or has been used:

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References

7. Curcumin C3 Complex® http://www.curcuminoids.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease

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