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NANOEMULSION- AN ANTIOBESITY DRUG

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ABSTRACT

Currently, obesity is a major health problem worldwide because of its rising prevalence and strong association with pathological disorders such as cardio vascular diseases, diabetes- type 2, hypertension, infertility and some forms of cancer. Nanotechnology has been developed into a multidisciplinary field of applied science and technology for target application. People prefer to take antiobesity drugs to reduce body weight rather than work outs. But these conventional drugs may cause adverse effects on heart and other organs. Nanoemulsion is considered as a potential drug delivery system with practical pharmaceutical applications. Oleoresin capsicum (OC) is an organic solvent extracted from dried ripe red pepper. The distribution of Nano Oleoresin capsicum (NOC) has particle size of 20 - 50 nm in diameter. In a rat study, NOC reduced the body weight and adipose tissue mass compared to OC as the action of NOC was on the target site.

INTRODUCTION

Health is the most important criteria for human beings in order to carry out day to day work. Physical health surely influences the mental health. Obesity is one such condition where in adipose tissue accumulates fat, if not taken care may lead to major health problems. Various ways can be adopted to reduce the body weight but in certain exceptional cases where weight reduction is a problem, nanotechnology based antiobesity drug can be used.

Nanotechnology

The word 'Nano' is derived from Greek word means 'dwarf or minute or microscopic' and product that incorporates such nanomaterial for dispensing of its properties and techniques used to make or design the nano product is called nanotechnology. Nanotechnology is the design, production and application of structures, devices, and systems through control of the size and shape of the materials at the nanometer (10^9 of a meter) scale where unique phenomenon enables novel applications (Ravichandran and Sasi, 2006). When particle size is reduced below this threshold, the resulting material exhibits physical and chemical properties that are significantly different from the properties of macro scale materials composed of the same substance. This technology was introduced by Richard Feynman in 1959.Nanotechnology is the ability to build and shape matter one atom at a time (Goodsell *et al*., 2004).

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Applications of Nanotechnology

Nanotechnology has been developed into a multidisciplinary field of applied science and technology for target application like pesticide encapsulated particles that releases the pesticide only in stomach of consumed insect preventing contamination in vegetables, fruits, pulses and grains; development of nano sensors and dispensers throughout the food crop field which sense the need for water, nutrients as deficient sensed by them before manual observations (Dingman, 2008). The nanocapsules that are incorporated with flavour, colour enhancers in food attracts the hungry consumers. The nanoparticle emulsion is used in icecreams and spreads to improve texture and uniformity (Miller, 2008). Food packaging involves edible, biodegradable nano wrapper which will envelope foods preventing gas and moisture exchange. It can be further used for detecting food spoilage saprophytes and pathogens such as *E. coli*, *Salmonella* spp and even to extend the shelf life by releasing nano-anti-microbials to food product (Richardson and Piehowski, 2008). Nano particles incorporated with nutrients in a capsule senses nutrient deficiency in body and their supplement was contributed by the nanosensors.

The nanoscience also contributed its applications in supplementing the enzymes, harmones and to control diseases such as diabetes, cancer (Sheng *et al*., 2013)

Obesity

Obesity is often defined as a condition of abnormal or excessive fat accumulation in adipose tissue, to the extent that health may be impaired (Garrow, 1988). It results from excess energy intake over energy expenditure. Currently, obesity is a major worldwide health problem because of its rising prevalence and strong association with pathological disorders such as heart disease, type 2 diabetes, hypertension, and some forms of cancer (Hill and Peter, 1998). The obesity problem is increasing day by day. As WHO estimation, 200 million people worldwide were with this problem in 1995-96, reached to 400 million in 2005-06 and were estimated to reach 700 million by 2015-16 [6]. Sedentary work, disturbed eating habits due to long working hours, disturbed sleep, over eating during stress, eating lot of junk foods with consumption of carbonated beverages, continuous use of certain drugs, hormonal imbalance are some of the factors that lead to obesity.In the field of food science, studies on obesity have focused on searching for food components that have the potential to suppress the accumulation of body fat and increase energy expenditure.

Control of obesity

Weight management can be done in various ways. Physical exercises at gymnasium, walking, yoga, running and jogging are some of the techniques to reduce the body weight but requires continuous work outs (Boutcher 2011). Mental preparedness with constant determination are very important for carrying out and follow ups in this method. Secondly, through the diet control which also should be done with great care and advice of dietician. Following this method for prolonged time is very difficult and further may end up with deficiency diseases. Lastly some of the drugs also help in reducing the weight but may lead to adverse effects. Numerous natural products, including crude extracts and isolated compounds from plants, have been linked to the reduction of body weight and prevention of diet-induced obesity.

Using Conventional drugs

There are two conventional drugs for treatment of obesity: Sibutramine (reduces fat by reducing food intake) and orlistat (a lipase inhibitor to decrease the absorption of fat in gastrointestinal tract). Emodin also found to be lipophilic hence reducing severity of fatty liver and lowering the lipid level (Jiang *et al*., 2001). Many pharmacological agents, including amphetamine, orlistat, rimonabant, and sibutramine, are used in the management of obesity. However, numerous drugs have been withdrawn recently, due to their adverse effects and risk of myocardial infarction, psychiatric disorders and stroke (Kang and Park, 2012). Among the alternative antiobesity medicines, conjugated linoleic acid (CLA) is considered to be effective. CLA is a fatty acid mixture of positional and geometric isomers of octadecadienoic acid (linoleic acid 18:2n-6) with a conjugated double-bond system (Wahle *et al*., 2004). To date, CLA has attracted interest as a weight-reducing agent because of its antiobesity activity due to reduced lipid accumulation in adipocytes via inhibition of lipoprotein lipase activity and decreased body fat mass via induction of apoptosis in adipocyte (Moloney *et al.,* 2014).

Antiobesity Nanoemulsion

A class of emulsions with a droplet size of 20–500 nm existing both water-in-oil and oil-in-water forms composing of surfactants or emulsifiers that are commonly used in food substances are termed as Nanoemulsions. The 1st nanoemulsion was introduced in 1940. Over the last few years, nanotechnology has been used in the development of nanoemulsions as pharmaceuticals over the last few years.In order to reduce the side effects, nanoemulsions are considered as potential drug delivery system with practical pharmaceutical applications (Kim *et al*., 2013). N-CLA showed a greater lipolytic effect on differentiated 3T3-L1 adipocytes compared with normal CLA. N-CLA enhanced the release of glycerol from triglycerides, which accumulated in differentiated 3T3-L1 adipocytes. Further, N-CLA enhanced leptin secretion to an extent similar to that of orlistat, an antiobesity agent. In an animal obesity model fed a high-fat diet, N-CLA attenuated accumulation of triglycerides, total cholesterol and low-density lipoprotein cholesterol in serum and also significantly decreased the volume of triglycerides and cholesterol in liver tissue. These results indicate that N-CLA has a greater antiobesity effect than CLA as a result of its improved bioavailability (Kim *et al*., 2014).

Another effective nanoemulsion antiobesity agent was prepared using *Oleoresin capsicum* (OC) which is an organic solvent extracted from dried ripe red pepper (Kim *et al*., 2013). It has been used in the preservation and enhancement of taste as it has little odour and a pungent taste. The ethanolic and butanolic capsicum extracts has various biological benefits, such as anti-cancer, anti-oxidant, and anti-inflammatory properties (Dwivedi *et al.,* 2011). OC contains numerous bioactive compounds such as acids, esters, alcohols, aldehydes, ketones, and carotenoid pigments, as well as capsaicin analogs exerting beneficial effects on health in cooperation with each other. OC application is limited due to its low solubility and poor bioavailabilityhas been observed in 3T3-L1 adipocytes that decreased glycerol- 3-phosphate dehydrogenase (GPDH) activity and CCAAT- enhancer-binding protein (C/EBP)-α and C/EBP-β mRNA expression thus leading to reduction in fat accumulation in adipose tissue. In order to increase bioavailability of OC, nanoemulsion delivery system available can be used (Zimmer *et al*., 2012).

NOC (Nano OC) was prepared by stirring 210g of OC with 201g of Tween 80 and dispersed into 2,100 mL of purified water with mild stirring for 1 hour. The coarse emulsion was passed through an air-driven Microfluidizer operated at 25,000 psi for five cycles. The microfluidized sample was dispersed into 2,500mL of 0.2% β-cyclodextrin solution for 2 hours using the syringe pump, and filtered with a 0.45 μm polyvinylidene difluoride filter membrane, then stabilized for 24 hours. The transparent solution was considered to be NOC. The control OC sample was prepared by dispersion of OC (210g), surfactant Tween 80 (201g), and 2,100 mL of purified water. The emulsion was then simply dispersed into 2,500 mL of 0.2% β-cyclodextrin solution without microfluidization. The distribution of the NOC particle size was between 20 and 50nm in diameter.The rats were randomly separated into three groups: a high-fat (HF) diet group, HF + OC diet group, and HF + NOC diet group. All groups were fed the diet and water

ad libitum for 14 weeks. NOC reduced the body weight and adipose tissue mass, whereas OC did not. OC and NOC reduced mRNA levels of adipogenic genes, including peroxisome proliferator-activated receptor (PPAR)-γ, sterol regulatory element-binding protein-1c, and fatty acid-binding protein in white adipose tissue. The mRNA levels of genes related to β-oxidation or thermogenesis including PPAR-α, palmitoyltransferase-1α, and uncoupling protein-2 were increased by the OC and NOC relative to the HF group. Both OC and NOC clearly stimulated AMP-activated protein kinase (AMPK) activity. In particular, PPAR-α, palmitoyltransferase-1α, uncoupling protein-2 expression, and AMPK activity were significantly increased in the NOC group compared to in the OC group. NOC decreased glycerol-3-phosphate dehydrogenase activity whereas OC did not. NOC could be suggested as a potential anti-obesity agent in obese rats fed a HF diet (Kim *et al.,* 2014).

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