

**Review Article**

**APPLICATION OF NANOTECHNOLOGY IN FOOD TECHNOLOGY AND TARGETED DRUG THERAPY FOR PREVENTION OF OBESITY: AN OVERVIEW**

**JYOTIBALA BANJARE**

Interactive Research School for Health Affairs, Bharati Vidyapeeth University, Pune (India)  
Email: jyotik.me@gmail.com

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**ABSTRACT**

Obesity is a medical condition arises as a result of an imbalance between lipolysis and lipogenesis which leads to accumulation of excess fat. Obesity is linked with major health complications such as diabetes, cardiac disorder, cancer, hypertension, sleep apnoea, etc. Weight loss through medication and healthy food balance can prevent obesity and associated disorders. Though, diet based therapy and drugs have short term effect with lacunae. At present, no reliable and established oral supplements are available to take care of obesity. Nanotechnology is a briskly emerging area of science and technology for food modulation at molecular and atomic level. The unique size and superior properties of nanomaterial have huge application in biology and medicine for food and drug development. Nanotechnology is playing an important role in the food industry for unindustrialized improved food, uptake, absorption, and bioavailability of nutrients to the body. Balanced or better-modified nutrients food, restricted calorie measures and commercial availability is geared through Nanoscience for control of obesity. Nanoparticle Targeted drug therapy, particularly for adipose tissue, may provide a new generation formulation for therapeutics of obesity.

**Keywords:** Nanofood, Nanomaterial, Drug delivery, Adipose tissue

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**INTRODUCTION**

The current epidemic of Obesity and associated number of chronic diseases are ultimately life threatening. The only solutions to obesity lies in altering lifestyle and food habits. The pharmacotherapy of obesity works through two ways; Appetite suppression (e. g., desoxyephedrine, phentermine); or the suppression of fat absorption (orlistat). Due to limited efficacy and unacceptable adverse effects like stroke and severe diarrhoea [1, 2] they are used strictly with limitations or withdrawn from the market. Nanoparticles are particle size less than 100 nanometres which exhibit novel applications and benefits. Nanotechnology can help in assembling materials into Nanoscale or adding Nano ingredient to food [3].

Food nanoparticles enter our bodies through different docks-nose, eyes, mouth, and skin. Foods, once broken down and digested, are absorbed at different levels of the alimentary canal. Absorbed food is in molecular scale size and, of course, enters all cells at different Nano dimensions. The emerging area of food technology together with Nanoscience and engineering improves functional food and delivery of the bioactive compound. Nanotechnology can produce novel food with altered properties and supplemented nutraceuticals for better health [4]. The mechanism and functionality of food is modulated in the ingredient, quality, taste, and packaging.

The safety and regulatory guidelines have also been reported [5] which open the new window for production of safe nanomaterial for the management of obesity. Consequently, there is prominence on replacing the fat in traditional foods using Nano ingredients that provide the distinguishing flavour, mouth feel and organoleptic properties of fat but then lack the high calories and risk factors accompanying with conventional fat [6].

Drug delivery involves manipulation of drug release, absorption, assimilation, distribution and elimination by influencing potential and safety of the drug. The binding specificity and targeting ability of nanoparticles to adipose tissue is most important in medical science for obesity control [7]. It has been reported that targeted delivery of nanoparticles in white adipose tissue of obese individuals enhances permeability and retention effect. It may prove to be masterwork in the development of new anti-obesity formulations [8].

Food supplements with added nanoparticles are becoming available worldwide. Fortification of food using nanotechnology produces food with boosted taste, modified colour, added nutraceutical, removed fat and sugar. The site (i. e adipose tissue) specific drug therapy will be novel approach for fat cell removal from obese. This article represents the overview of a food nanotechnology on low-fat food manufacture and role of nanoparticles for targeted drug therapy in obesity management.

**Nanotechnology in food modulation**

The food industry has begun to realise the full potential of nanotechnology. Food that is cultivated, produced, processed or packaged using nanotechnology is termed 'Nanofood' which is composed of nanomaterial [9]. Research have claimed that Nano-sized nutrients and supplements possess a greater uptake, absorption and bioavailability in the body compared to similar volume substance. Such feature of nano-particles itself attracted a lot to commercial interest in manufacturing of nano-sized ingredients, supplements and nutraceuticals. Currently applications of nanotechnology span a wide range of sectors, predominantly personal-care, health-care and cosmetics [10]. The benefits of nanotechnology in the food sector is through the whole food chain, starting from production to processing, transportation, safety, storage and delivery. Nanoparticles basically belong to the group of colloids (like; emulsions, micelles, mono-and bilayers). In another word, nutrient and additive preparation, encapsulation (additive/nutrient, flavour/colour, enzymes), structure control [texture, heterogeneous mixtures (emulsions, suspensions)] are an application to produce food in nanotechnology. Compound with higher properties of proper absorption, digestion, and easy passage to the gastrointestinal tract (GI) have been manufactured (fig. 1) for various application in pharmaceuticals and food industries [11].

The food produced by nanotechnology can be categorized based on properties, processing (heat/mass transfer, nano-scale reaction engineering, Nano-biotechnology, and molecular synthesis), product (delivery, formulation, and packaging), materials (Nano-particles, Nano-emulsions, Nano-composites, and Nanostructures materials), food safety and biosecurity (Nano-sensors and Nano-tracers) [12]. Nanofood has been a part of food processing for centuries, by means of the food structures that naturally exist at the Nanoscale. In 2000,

Kraft Foods started the first nanotechnology laboratory "Nanotek", it was estimated that there are more than 180 applications of nanotechnology in various stages of development in food industry worldwide. A survey of nanotechnology-based consumer products on the market estimated that over 200 manufacturer-identified "nano" consumer products which are currently available, and about 59 and 9% of the products are categorised as "Health and Fitness" (largest main category) and "Food and Beverage" products, respectively [13].

Nanofood is developed to improve food safety, enhance nutrition, flavour, and cut costs. This technology to also employ to produce

low-calorie food with better taste, appearance, functionality aided with nutritional supplement by altering the sugar and salt content in food [14]. Based on the current state of knowledge, the debate on the benefits and risks of applying nanotechnology in the food industry will last long. Although there are currently no conclusive data about the undesirable results of nanotechnology, it is probably wise to take a precautionary principle to deliberate the possible regulatory control as a proactive approach until proven otherwise.

Regulation on the use of nanotechnology in food systems is, therefore, necessary for managing the potential adverse effects of nanotechnology and protecting the public [15].

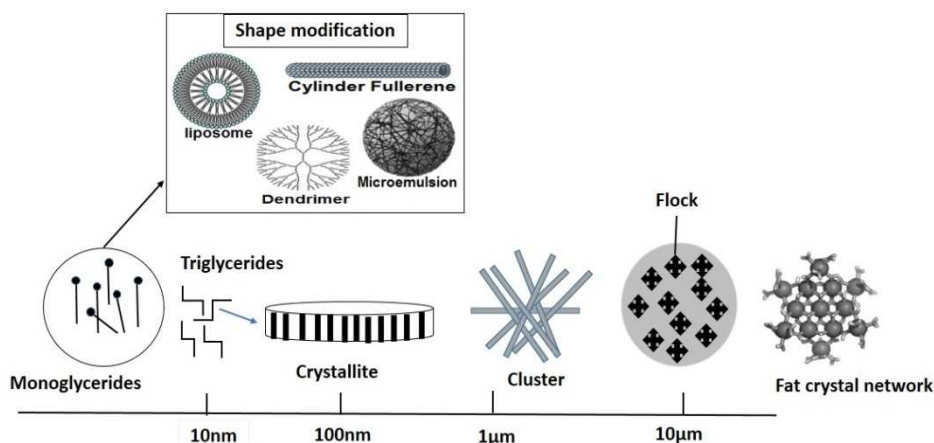


Fig. 1: Modification of triglyceride (fat) using food nanotechnology

#### Nano derived food products for obesity prevention

The tempting tastes of fat and sugar attract all age groups including children, Adolescents, and young adults. Unfortunately, the food that tempt taste bud is high calorific and unhealthy. The goal of nano-derived food is to achieve eatables which are calorie binder with complete and better bioavailability antioxidants. The delivery of nanoparticles for fat replacement takes place in three ways-lipid-based where a long chain of fatty acids are replaced by small chains, and its absorption of fat and cholesterol is also reduced. In protein-based, food with reduced energy content are produced. The polysaccharides-based, low energy density calorie compact food are produced [16]. The Nano derived food products of modified fat or synthetic fat are:-

Low sweetener cold drinks, milk, low fat cheddar cheese, spreads, ice-cream, chocolates, yogurt, kefir (a cultured milk Beverage), tempeh (made from soybeans), and kimchi (a Korean fermented cabbage dish) [16].

Vitamin B<sub>12</sub> spray that can be directly sprayed into the mouth to fulfil the need of essential fruits and vegetables, it is directly absorbed by mucosal cells [17]. Some available functional food are coenzyme-Q10 and nanocapsules of omega-3 fatty acids [18]. According to researchers hot chips, cookies and chocolate cookies will be soon available in markets. Nano salt, Nano milk, fat reduced mayonnaise and meat are under development [19]

Nano derive fat-free food aims to deliver food that makes the consumer feel full without overeating. The immediate breakdown of fatty food into emulsion before reaching ileum crops immediate satiety after a meal. In many countries, food, food products, and food packaging materials based on nanotechnology are already available to consumers (As shown in table 1), and it is probable that nanotechnology-derived low-fat food products will be progressively available to consumers worldwide in future [20].

Table 1: Modified nano food for weight reduction

Modified nano food products	Potential application
Canola Active Oil	Provides vitamins, minerals, and phytochemicals
Nanotea	Improve selenium uptake
Nanocuticals Slim Shake Chocolate	Low fat
Nano silver, nano gold	Mineral supplements
Carotenoids nanoparticles	Fruit drinks for improved bioavailability
lycopene, beta-carotenes and phytosterols	Prevents accumulation of cholesterol
Milk caseins	lowers serum cholesterol
Meat	Replacement to meat's cholesterol
High-oleic soybean	Polyunsaturated fatty acids were reduced upto 70%
Sorbitol and trehalose	Calorie-free or low-calorie sugars substitutes for sucrose in
Vitamins such as thiamine, riboflavin, niacin or folic acid	Increase the content as well as the bioavailability
Salatrim, an acronym for short and long chain acid triglyceride molecules.	Replaces fat in chocolate, confections, dairy products, frozen desserts, and cookies.
Olestra	Synthetic low calorie fat

## Nanoparticle drug delivery system

Nanoparticles are designed for drug delivery systems usually as lipid or biodegradable polymer-based to improve the pharmacological and therapeutic properties of drugs administered parenterally. Biodegradable polymeric nanoparticles majority reported so far have dealt with microparticles created from poly(D,L-lactide), poly(lactic acid) [PLA], poly(D, L-glycolide) [PLG], poly(lactide-co-glycolide) [PLGA], and poly-cyanoacrylate [PCA] for drug delivery and tissue engineering, for controlling the release of drugs, stabilizing labile molecules (e. g., proteins, peptides, or DNA) from degradation, and site-specific drug targeting. The aims for nanoparticle entrapment of drugs are either enhanced delivery to, or uptake by, target cells and/or a reduction in the toxicity of the free drug to non-target organs [21].

### Targeted drug delivery in obesity by nanoparticles

Nanoparticles have proven to be effective in the treatment of particular locations of the body through targeted delivery system. They work efficiently enhancing half-life of drug molecules, regulatory particle size, surface character; enhance permeation, flexibility, solubility and release of therapeutically active agents in order to attain the target and specific activity at a controlled rate and time. [22].

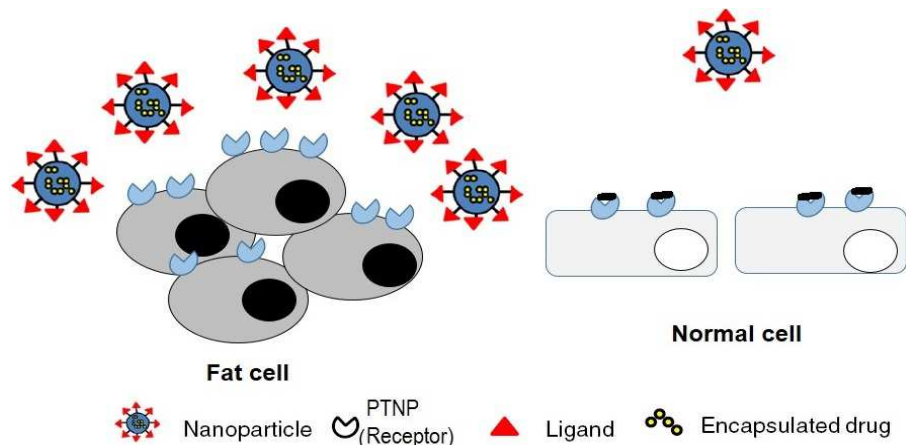
Nano drug molecules bind to proteins found in the lining of the blood vessels that surround adipose tissue or binds to receptors on the outer surface of the adipose tissue and burn it. Study have shown that promoting the growth of new blood vessels, a process is known as angiogenesis, can help transform adipose tissue and lead to weight loss in mice. Though, drugs that promote angiogenesis can be harmful to the rest of the body and further investigation is required to target fat cell with low drug side effect [23]. A study in a diet-induced mouse model showed that a programmed death of

endothelial cells by antiangiogenic drugs (TNP-470) removes vascular tissues effectively reduces weight in animals [24].

A study in high-fat diet animal model has demonstrated that natural resources like Chitosan (CTS), water-soluble chitosan (WSC), microparticles (MPs) and nanoparticles (NPs) reduces weight and retains safety standards which is very important for weight management in humans [25]. Previously it was shown that Superparamagnetic iron oxide nanoparticles (SPIONs) revises the expression of various genes responsible for obesity-associated type 2 diabetes hence play an important role in adipocyte prevention. The magnetic nanoparticles is applicable as a tool of drug delivery trajectories and is a promising technology for the treatment of various disease. Magnetic nanoparticles products are already available in markets [26].

Both *in-vitro* and *in vivo* study on Nanoparticle (Nanoceria) has proven to interfere with the adipogenic pathway by reducing the mRNA transcription of genes involved in adipogenesis (formation of adipocyte), and by lowering the triglycerides accumulation in 3T3-L1 pre-adipocytes. Nanoceria in Wistar rats have not standard toxic effects, but effectively worked on reducing the weight gain and also lowering the plasma levels of insulin, leptin, glucose and triglycerides [27]. Human adipose tissue is highly vascularized and poses anti-angiogenic properties. A pro-apoptotic peptide ligand bound with significant nanoparticle/nanocarrier which is delivered to obese adipose tissue causes depletion of endothelial cells increasing cell apoptosis [28] (as shown in fig. 2).

It can be promising in future to control obesity by using nanotechnology for targeted vascular therapy as an anti-angiogenic agent. Based on the passive drug delivery approach numerous nanotechnology formulation have been approved by FDA in US.



**Fig. 2: Targeted drug delivery in adipose tissue. The smart drug delivery system enhances the polymer nanoparticle better stage to their therapy regimen**

**Table 2: Proapoptotic ligand modified liposomal with nanocarriers for obesity control**

Pro-apoptotic ligand	Nanocarriers	Effect in obesity
<i>[D(KLAKLAK)2, KLA]</i>	<i>Prohibition targeted nanoparticle (PTNP)</i>	Reduced body weight in diet-induced obesity mice model.
<i>Cytochrome (Cyt C)</i>	<i>PTNP</i>	Reduction of obesity in high-fat diet mice model
<i>Poly(ethylene glycol)2000</i>	<i>PTNP</i>	Significant reduction in diet-induced obesity
<i>Poly(ethylene glycol)5000</i>	<i>PTNP</i>	Substantial reduction in diet-induced obesity

It can be proposed from the finding shown in table 2 that PTNP, which is expressed in the endothelial cell surface of the adipose tissue of humans [29] is the most important nanocarrier in vascular target drug design. The development of low dosage drug can be truly beneficial in the clinical application for obesity control.

### Nanoparticle and surgical weight loss

NanoLipo, a unique area for weight loss procedure, is under research which is directing to develop a safer and more effective

alternative to traditional liposuction by using gold nanoparticles. Fatty areas are injected with a solution containing nanoparticles of gold. The area is then treated with a laser with an 800-nanometer wavelength (similar to the kind used in laser for hair removal). The gold nanoparticles react to laser and begin to emit heat rapidly. Fat melts at lower temperatures than the surrounding connective and nerve tissues-so only fat cells are liquefied. The melted fat will be then removed through needle [30].

## DISCUSSION

Obesity is rapidly increasing worldwide according to WHO and also the risk factors associated to it. The prevalence is almost equal in all types of countries and economic status [31]. Food is what, like to eat, salty, sweetener, larger volume and crunchy taste which shows the path of unhealthy and junk food and ultimately weight gain. Nanotechnology reduces the size of food, amount of calories and provides well-adjusted bioactive compounds. Small size with good shelf life fresh packing, low cost, high potential and minimal or no side effects makes it a good choice for consumers [32].

As per Kim at the International Nanofood Research Society in Seoul, South Korea there are several additional Nano methods available in spite of low-calorie food for obesity prevention [33]. The expected outcomes of this Nano approach is healthier life, improved taste, fewer medical costs concerning diet-related diseases, commercial gain, efficiency, less drug dose due to higher efficacy of drugs, and healthy population [34].

The biocompatibility and biodegradability property of various natural and synthetic polymers mainly Poly (lactic acid) (PLA), Poly(glycolic acid) (PGA), and their copolymers (PLGA) led to extensive study for the preparation of potential carrier nanoparticles for drug therapy in various health ailments including obesity. The researchers had shown that when overweight mice were fed an excessive fats food, later injected with polymers PLGA then, the animals managed to lose 10% of their weight in the course of the 25 d of therapy [35].

Mainly nanotechnology applications are engineered nanoparticles (ENPs) that are manufactured specifically to attain a definite material property or composition. The use of insoluble (or indigestible) ENPs in food applications, such as certain metal (oxide) ENPs that are unlikely to be assimilated inside or outside the GI tract raises a number of consumer safety concerns. Thus the magnitude of hazard, exposure and hazard from the ingestion of ENPs via food and drink are largely unknown [36]. A previous study has reported an *in vitro* study using SiO<sub>2</sub> nanoparticles on human epithelial cell cultures that a nanoparticle can enter into the cell nuclei and leads to impairment of DNA replication as well as transcription. SiO<sub>2</sub> nanoparticles are commonly used as a food additive and likewise in food packaging [37].

Nanotechnologies manufacture standard ingredients such as salt, fat and biopolymers to produce foods with improved properties which usually be broken down in the body in the usual way. Some examples of inorganic nanoparticles that could poses a risk include silver, titanium and silica, which are difficult to intake and metabolised in body system naturally. Thus, it is certainly serviceable for the food and drink industry to look at the use and safety of these inorganic nanoparticles. The use of silica nanoparticles as centres for diet products, such as the commercial Chocolate Slim Shake, can raise concern for regulation in a proper manner.

A variety of biological substances like albumin, gelatine and phospholipids for liposomes are presently under analysis for the preparation of nanoparticles for drug delivery and certain substances of a chemical nature like polymers, and solid metal nanoparticles are also under examination. It can be assumed that the potential interaction with tissues and cells, and the potential toxicity, greatly depends on the genuine composition of the nanoparticle formulation [38]. Conversely, nanoparticles may lead to possible hazards to larger cell particles (eg, mitochondrial damage, uptake through the olfactory epithelium, platelet aggregation, and cardiovascular effects). The effects illustrated clearly need a new way of handling their toxicology. Epidemiological evidence suggests that these effects occur mainly in subjects with impaired health. This finding should be amended in developing varied toxicological testing models [39]. The combination of potential harms and benefits of nanotechnology, regulatory consideration for public concerns regarding the probable inadvertent consequences of this new technology (from negative human and environmental impacts to questionable health and surveillance applications) should be considered [40].

Obesity prevalence is higher in countries with limited resources while nanotechnology requires a well-equipped lab which limits the use of this technology all over the world equally. Nanotechnology is a laboratory technique and cannot be compared with natural products with its natural efficiency. All products derived from nanotechnology required to be studied well before commercial implication. Nanotechnology is unique laboratory technology, so it requires extensive research to approve its safety against society and environment. The site-specific nanomaterial targeting methods need to monitor in order to avoid capturing of organs like liver and spleen.

## CONCLUSION

Opting low-calorie, low-fat food has become a priority to the obese consumer, but long term diet programme have innumerable consequences. Food Nanotechnology is a new areas for producing food with complete functionality and sensory qualities. According to researchers, Nanotechnology will revolutionise the entire fat food products in future. The low calorific and sugar junk blocked food will significantly reduce weight and improve the quality of life. Nanotechnology-based drug delivery in the obese adipose tissue will enhance opportunity in the pharmaceutical industry. The extensive study targeted drug therapy will provide new breaks in the pharmacotherapy of weight management. Nano therapy can be a door to new anti-obesity formulation with the systematic and advanced administration. It can revolutionise the clinical trials and understanding of vascular targeted drug delivery for obesity control. Nanofood is engineered and prepared under extensive laboratory set up which may attest it puzzling for consumer care and recognition from FDA. The public acceptance of food nanotechnology for obesity prevention is based on the quality and safety assurance provided by the administration, manufacturers and concern expert. Although there is the huge application of nanotechnology in food technology, but exploring new anti-obesity formulation at nano size level and making it commercially accessible needs to study unbreakable by researchers.

## CONFLICT OF INTERESTS

Conflict of interest declared none

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