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Tackling obesity from a nanomedicine perspective

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Abstract
Obesity is a worldwide issue that is progressively worsening. It can result in significant co-morbidities, including type 2 diabetes, cardiovascular disease, and obesity-related cancers. Current treatment options for obesity have several limitations, and the connection between obesity and cancer development is not well comprehended. We examine the current state and future prospects of obesity therapy, with a focus on the potential application of nanomedicine. The presentation emphasizes the necessity for further research in this field and how developments in cancer therapy using nanomedicines could be applied for the treatment of obesity, thereby providing a safe and effective treatment with reduced side-effects for those patients.

KEYWORDS
cancer, adiposopathy, magneto-mechanical stress, hyperthermia, nanomedicine

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MAIN MESSAGE

According to the World Health Organisation, obesity is defined as a body mass index (BMI) greater than 30 kg/m^2. Recent projections indicate that more than 1 billion people will be obese by 2030. Currently, there are approximately 500,000 deaths annually in the United States of America from obesity-related diseases. Obesity is a preventable and reversible chronic disease that predisposes patients to comorbidities due to underlying biological stresses such as chronic inflammation and the generation of reactive oxygen species (ROS) [1] that are associated with the disease. Common comorbidities include type 2 diabetes mellitus, dyslipidaemia, osteoarthritis, and coronary heart disease, but cancer is rarely mentioned or recognised as a serious comorbidity of obesity worldwide [2]. Obesity increases the likelihood of developing at least 13 different types of cancer (e.g. endometrial, pancreatic, breast, and colorectal), which equates to 200,000 new cases diagnosed each year [1]. In the US, approximately 14% of cancer deaths in men and 20% in women are attributed to patients who are overweight or obese [3]. Obesity constitutes an important determinant of cancer mortality, and intentional weight loss is the most effective way to reduce the risk of obesity-related cancers [3].

A balanced, low-calorie diet and an increased

physical activity are the cornerstones of obesity treatment and are essential to reduce energy intake and increase energy expenditure. However, lifestyle changes are challenging for patients due to genetic, biological, and environmental factors that affect long-term adherence. When lifestyle changes alone are not sufficient, adjunctive treatments are available. However, although a 5%-10% reduction in body mass can be achieved, those treatments are associated with unpleasant side-effects, and the failure rate of weight loss therapy is extremely high (90%), further reducing its prospects of reducing the prevalence of obesity and obesity-related comorbidities. Bariatric surgery and weight loss devices are highly invasive procedures that require intensive monitoring for life-threatening complications [4]. Therefore, new strategies are urgently needed to safely reduce the prevalence of obesity and its impact on obesity-related cancers. By integrating knowledge from already approved nano-based cancer therapies, anti-obesity nanomedicine can be developed and improved, thus reducing the future risk and mortality of obesity and obesity-associated cancer [5]. The similarities between adipocytes and cancer cells are characterised by their dysfunctional cellular behaviour [6]. During adipose tissue hypertrophy, adipocytes have high proliferation rates, and compromised vasculature and increased angiogenesis is developed, which are consistent with hallmarks of cancer growth [5]. Proinflammatory cytokines, chronic inflammation, and ROS generation from excess fatty acid influx are *bona fide* tumour promoters, and illustrate how increased weight gain contributes to an increased risk of tumour development [5]. In addition, the adipose tumour microenvironment enhances tumour survival and evasion of the host immune system [7]. This results in decreased survival and increased treatment complications in patients with cancer and obesity [6].

This presentation highlights the strong evidence for the use of nanomedicine in the treatment of obesity due to the improved safety and efficacy of advanced nanocarriers. For example, a nanoemulsion of orlistat developed by Chen *et al*. [8] showed a reduction in the incidence of adverse effects while reducing weight gain in a diet-induced obesity mouse model. Other organic nanocarriers have been investigated for the development of anti-obesity phytochemicals. The presentation focuses on the use of inorganic nanoparticles such as superparamagnetic iron oxide nanoparticles (SPIONs), which are FDA-approved inorganic nanomaterials with a good biodegradability, to combat obesity by providing examples from our research and the literature. We use a magneto-mechanical approach to induce oscillation of SPIONs by applying an alternating magnetic field to cause cell damage. Previous studies have shown that a high alternating magnetic field can cause significant delipidation of adipocytes through thermogenesis, with no signs of damage or mutation observed [9]. SPIONs can be administered orally or directly, and can be optimised for theranostic purposes. They can perform both magnetic resonance imaging and drug delivery.

Anti-obesity nanomedicine is still in its infancy, but as noted above, it has promising potential to reduce the development of co-morbidities, decrease patient mortality, and improve quality of life. The reduction in obesity prevalence could alleviate the financial burden on healthcare systems. Potential gaps for anti-obesity nanomedicine to reduce the incidence of obesity include managing drug-induced weight gain, improving the affordability, tolerability, and accessibility of treatment in a high-demand “rapid weight loss” market, or use in patients with morbid obesity.

Although there are several challenges to clinical translation, there is great promise for improving obesity therapy through nanomedicine developments in the near future. A more effective weight loss therapy could have a significant positive impact on obesity-related cancers, financial costs, and metabolic disorders, while it could also slow the increasing trend of obesity worldwide.

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CONFLICT OF INTEREST STATEMENT

The author declares no conflicts of interest.

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