Effect of fatty acid(s) extracted from marine topse (*Polynemus paradiseus*) fish oil on obesity and obesity related metabolic disorders

Abstract

Obesity is a major public health concern, and its prevalence is growing alarmingly on a global level. Obesity is determined by genetic, neurological, metabolic, gastrointestinal, and behavioural factors which are connected with the number of comorbid abnormalities, such as cancer, diabetes mellitus, and cardiovascular disease. Consumption of fish has become popular in regular meals. Current research has demonstrated that marine fish oil (FO) may offer an alternative method because of their significant health benefits for lowering obesity and its related issues. Marine FO enrich in long- chain omega- 3 polyunsaturated fatty acids (LC n- 3 PUFA), long- chain omega- 6 polyunsaturated fatty acids (LC n- 6 PUFA) and monounsaturated fatty acids (MUFAs) performs a crucial role in decreasing metabolic syndrome abnormalities and has a number of disease combating properties, including cardioprotective, anti-atherosclerotic, anti-obesity, anti-cancer, and anti-inflammatory activities. Considering the adverse effects of marketed drugs (orlistat, lorcaserin, liraglutide, semaglutide etc), to minimize the risk of obesity, we extracted, isolated and characterized marine *Polynemus paradiseus* FO in this investigation for the first time. Marine *P. paradiseus* fish widely found in the Eastern Indian Ocean and Western Pacific region including India, Thailand, Myanmar, Bangladesh and Pakistan. This fish locally named as topse fish are indigenous source which highly thrives in West Bengal's marine areas in India also. Due to limitation of biological activities on *P. paradiseus* FO, we design *in vivo* model experiment to investigate the efficacy of marine *P. paradiseus* FO in treating obesity-related metabolic diseases. In our experiment, compared to the high fat diet (HFD)-induced obese control (OC) group, the *P. paradiseus* FO supplemented obese mice group (Treatment-I and Treatment-II) represented a remarkable reduction in body weight, body mass index (BMI), and serum lipid profiles. The FO-supplemented HFD-induced obese mice group demonstrated an average diminution in obesity and inflammatory-related adipocytokines in FO supplemented groups compared to the OC group. *P. paradiseus* is a reasonable choice since it contains a significant number of essential fatty acids such as 51.15 % of PUFAs including methyl ganma-linolenate, methyl linolelaidate, DPA, methyl arachidonate, DHA etc, and 25.04% of MUFAs such as methyl cis- vaccenate, gondoic acid, methyl cis-11-icosenoate, and methyl cis-12-octadecenoate etc and its physicochemical features confirm that it is harmless for human

ingestion. Among all the MUFAs present in *P. paradiseus* FO, Gondoic acid (GA), has been considered as a possible substitute for fish-derived fatty acids, its function in molecular level and adipocyte proliferation remains unclear. Present research examines the anti-obesity efficacy and mechanisms of GA treatment in HFD-induced obese mice and adipocyte development in 3T3-L1 cells, presenting an innovative research viewpoint in a current topic of research. Our findings, explored that administering GA reduced body weight, serum lipid profile levels, modified inflammatory responses and adipogenesis in diet-induced obese mice. From *in vitro* study, cellular viability assay was performed to investigate possible cytotoxicity of GA. In a culture of matured 3T3-L1 adipocytes, lipid buildup was evaluated using Oil Red O (ORO) staining and triglyceride accumulation (TG). Adipogenic transcription parameters were used to assess adipocyte differentiation, and semi-qPCR was performed to examine the regulation of lipid metabolizing genes. GA's anti-adipogenic impact was caused by the reduction of adipogenic transcription factors such as sterol-regulatory element binding protein-1c (SREBP-1c) and peroxisome proliferator-activated receptor gamma (PPAR-γ) and also reduced the expression of lipid accumulation gene, fatty acid synthase (FAS). In HFD-induced mice, GA treatment enhanced glucose sensitivity, lowered fasting insulin levels, and altered adipocytokine levels, enhancing thermogenesis and β-oxidation in mitochondria via the AMPK mechanism.

In conclusion, our overall study explored that *P. paradiseus* FO enriched with a significant number of essential fatty acids (FAs), it may be employed as a nutritional supplement to combat obesity. Secondly, *P. paradiseus* FO derived GA showed inhibition of adipocyte development, lipid build up in 3T3-L1 cells. Our research also explored that the treatment of 4 mg GA supplementation with the duration of 35-42 days may serve as an effective strategy to mitigate obesity associated metabolic dysfunction by enhancing browning, reducing lipogenesis, improving some of the metabolic and insulin signalling abnormalities linked with HFD feeding.

Keywords: obesity, essential fatty acids, gondoic acid, preadipocyte cell, metabolic imbalance, TG accumulation, mitochondrial biogenesis