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Effects of Orlistat and herbal mixture extract on brain, testes functions and oxidative stress biomarkers in a rat model of high fat diet

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ABSTRACT

This study was designed to assess the effectiveness of herbal mixture extracts of pumpkin seed oil, peanuts shell and Orlistat on brain, testes functions, oxidative stress biomarkers and histopathological changes in male albino rats administered high fat diet. Fifty male rats were divided into four groups: 1st administered normal diet, 2nd administered high fat diet, 3rd administered high fat diet with Orlistat and 4th administered high fat diet with herbal mix.

A group of rats were fed with a standard control diet (1st control group was 12 rats for 22 weeks) and another group of rats were fed a diet containing 35% fat (2nd high fat diet) for 16 weeks. Then, this group of high fat diet was divided into 3 groups for the following 6 weeks: 1st group administered high fat diet only (13 rats), 2nd group administered high fat diet plus 2 mg/kg bw/day Orlistat (12 rats) and 3rd group administered high fat diet plus 5 mg/kg bw/day pumpkins and 2 mg/kg bw/day peanut shell extract (13 rats). Blood samples, brain and testes tissues were collected for biochemical assays and histopathological studies.

High fat diet group showed a high significant increase ($P < .001$) in feed intake, body weight and body mass index. HFD showed a significant increasing in Nor Epinephrine, Dopamine, BCHE, Homocysteine and malondialdehyde contents in brain. In testes high fat diet increased malonaldehyde contents of testes. An improvement by the treatments with Orlistat and herbal mixture was observed. Histopathological examination of brain and testes sections of high fat diet rats supported the previous biochemical results.

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We concluded that the treatment with Orlistat and herbal mixture ameliorated the harmful effects of the high fat diet and reduce feed intake.

1. Introduction

Obesity had been one of the leading public health concerns in industrialized societies for the last 40 years. It had been defined by the WHO as a body mass index above 30 kg/m^2 (WHO, 2006). It was reported that obesity increased the risk of neurodegenerative diseases, such as the degradation of neural membrane glycerophospholipids, the disruption of protein synthesis, degradation and the generation of reactive oxygen species (Kawarazaki et al., 2010). While treatment with Orlistat showed that alteration of the various hypothalamic neuropeptides' Central nervous system (CNS) levels, or alter the key CNS appetite monoamine neurotransmitters' levels that will suppress appetite. Also, treatment with herbal mix (PO) improved the brain from damage due to its content of omega-3 fatty acids. Goncalves et al. (2005) demonstrated that omega-3 fatty acids modulate changes in the concentrations and actions of several orexigenic and anorexigenic neuropeptides in the brain, including neuropeptide Y, alpha melanocyte stimulating hormone and the neurotransmitters serotonin and dopamine. But in case of PES, luteolin that found in peanut shell extract effectively produce a natural anti-inflammatory effect that stops the errant microglial cells from causing damage, protect cell neurons from damage and inhibited the production of neurotoxic inflammatory mediators (Benson, 2010) and is significantly increased the activities of Superoxide dismutase (SOD), Catalase (CAT) and decreased the levels of Malonaldehyde (MDA).

Also, it was reported that obesity is a cause of male infertility (Du Plessis et al., 2010). As morbidly obese males present with excess scrotal fat. The environmental toxins that accumulate in the white adipose tissue surrounding the scrotum might have a direct localized effect on spermatogenesis in the testes lipophilic contaminants are associated with decreased sperm production and thus decreased male reproductive potential. It was found that men with a body mass index greater than 25 kg/m^2 had a lower total sperm count than men of normal weight (Aggerholm et al., 2008). Belong to oxidative stress; it was known that obesity increased oxidative stress in reproductive system that defined as stress induced by increased numbers of molecules containing free oxygen. While treatment with Orlistat showed a high significant decrease in testes MDA level (Yesilbursa et al., 2005). Also, with treatment with herbal mix showed improvement in sperm count and testicular histology. This could be due to antioxidative properties such as tannins and vitamin A present in the oil (Nkang et al., 2003). Vitamin A protects the testis against lipid peroxidation, hence, promotes spermatogenesis and improves structural differentiation of epithelial cells of the epididymis. This study investigates effect of an obesity-associated risk factor on brain and testes oxidative stress, its mechanism of action and biomarkers associated with the effect of Orlistat and herbal mixture on it.

2. Material and methods

2.1. Materials

2.1.1. Diet

Two types of diets had been used, control rat chow diet and special High fat diet (HFD) (35%) for induction of obesity in rats:

a ***Normal rat chow diet:*** It was formed according to Kim et al., 2004. The standard normal rat pellet chow consists of concentrate (350 g), corn (600 g), calcium carbonate, dicalcium phosphate, sodium chloride magnesium oxide and vitamins (50 g). Standard normal rat diet composed of 65% CHO (60% starch+5% sucrose), fat 5%, crude protein 20%, vitamins and minerals 5%, fibers 5%, metabolic energy of this diet is 2813 kcal/kg with 8% from fat.

b ***The high fat diet:*** composed of 300 g concentrates, 350 corns, 300 g beef tallow, 50 g vitamins, minerals and fibers according to Kim et al., 2004. Percentage of HFD was 20% crude protein, 35% fat, 40% CHO (starch 35%, 5% sucrose) 5% vitamins, minerals and fibers. Metabolic energy of this diet is 5130 kcal/kg, 61% of this energy from fat. HFD would be lard, sunflower oil and starch for induction of obesity from local market by adding 30% lard or beef tallow and 5% sunflower to the control diet (Kim et al., 2004).

2.1.2. Chemicals

Orlistat is a white to off-white crystalline powder. Orlistat is practically insoluble in water, freely soluble in chloroform, and soluble in methanol and ethanol. Orlistat is available for oral administration as a dark-blue or turquoise hard-gelatin capsule. Each capsule contains a pellet formulation consisting of 120 mg of the active ingredient, Orlistat, as well as the inactive ingredients microcrystalline cellulose, sodium starch glycolate, sodium lauryl sulfate, povidone, and talc (The internet drug index RxList, 2012). Orlistat is (S)-2-formylamino-4-methyl-pentanoic acid (S)-1-[[(2S,3S)-3-hexyl-4-oxo-2-oxetanyl]methyl]dodecyl ester. Its empirical formula is $C_{29}H_{53}NO_5$, and its molecular weight is 495.7. It was given orally by oral gavage with a dose 2 mg/kg bw/day (Kumar and Alagawadi, 2010).

2.1.3. Herbal mixture

Mixture herbal extract of *Arachics hypogaea* nutshell extract and cucurbitamoschata plus morus alb (Moreno et al., 2006) from local market.

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