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## Genetics and epigenetics of cardio-metabolic complex diseases

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The metabolic syndrome (MS) constitutes a combination of underlying risk factors for an adverse outcome, cardiovascular disease. Thus, the clinical behavior of the MS can be regarded as a whole. Nevertheless, from a pathogenic point of view, understanding of the underlying mechanisms of each MS intermediate phenotype, obesity, hypertension, type 2 diabetes and particularly insulin resistance is a difficult task. Systems biology introduces a new concept for revealing the pathogenesis of human disorders and suggests the presence of common physiologic processes and molecular networks influencing the risk of a disease. It will be showed a model of this concept to explain the genetic determinants of MS-associated phenotypes. Based on the hypothesis that common physiologic processes and molecular networks may influence the risk of MS disease components, we propose systems-biology approaches i.e. a gene enrichment analysis and the use of a protein-protein interaction network. Our results show that a network driven by many members of the nuclear receptor super family of proteins, including retinoid X receptor and farnesoid X receptor (FXR), in addition to Clock, SLC6A4, PGC1A, etc, may be implicated in the pathogenesis of the MS by their interactions at multiple levels of complexity with genes involved in metabolism, cell differentiation and oxidative stress. In addition, it will be discussed alternative genetic mechanisms that are gaining acceptance in the physiopathology of the MS components, in particular fatty liver disease: the regulation of transcriptional and post-transcriptional gene expression by micro-RNAs and epigenetic modifications such as DNA methylation of not only nuclear but mitochondrial genes.

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## Potential anti-obesity and hypolipidemic assessment of *Orthosiphon stamineus* in animal model of obesity

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The obesity incidence has increased at an alarming rate in recent years, becoming a worldwide health problem. Due to the serious adverse effects of available anti-obesity drugs and some success of identifying natural products for overcoming obesity, more researches have been focused on the identification of natural products with less unpleasant adverse effects. *Orthosiphon stamineus* Benth. or java tea, is traditionally used to treat various disorders. Therefore, this study investigated the anti-obesity and lipid lowering activity of *O. stamineus* (200 and 400 mg/kg) on high-fat diet (HFD) induced obese mice. The oral administration of *O. stamineus*, for 8 weeks, resulted in a significant decrease in body weight gain in mice fed a high-fat diet. Subsequently, the food intake between the treatment and the HFD groups were similar which suggested that *O. stamineus* did not suppress appetite. Moreover, administration of *O. stamineus* significantly reduced the serum triglycerides, total cholesterol, low-density lipoprotein cholesterol, and liver oxidative stress levels compared to the HFD control group. Besides, the *O. stamineus* extract treatment elicited a significant reduction of serum glucose, insulin, leptin and adiponectin levels compared to that of the HFD control. The present study thus concludes that *O. stamineus* can possess hypolipidemic and anti-obesity activity that protects the body against adverse effects of high fat diet-induced obesity, possibly through suppression of body weight gain, lipid lowering action, improvement in insulin and leptin sensitivity.

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