



## Editorial

# Indian spices and Caffeine treatment for Obesity and Cardiovascular disease

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## Editorial

The global obesity epidemic that was previously reported [1,2] is now to worsen with obesity to double in 73 countries around the world [3,4]. Improving the health of obese individuals by dietary restriction, anti-obese foods and increased physical activity [1] has not reduced the global obesity epidemic. Obesity is linked to nonalcoholic fatty liver disease (NAFLD) [5,6] with complications relevant to the metabolic syndrome and cardiovascular disease [7]. Appetite control has become critical to endocrinology and metabolism with the apelinergic pathway and nuclear receptor Sirtuin 1 (Sirt 1) now connected to the endocrine system [8] and critical to metabolism. The apelin-Sirt 1 interaction involves nitric oxide (NO) [9] that is now considered as the defect [10] in the interaction between the peptide apelin and calorie sensitive gene Sirt 1 involved in NO imbalances in the adipose tissue, liver and the brain.

A model proposed involves the central co-ordination of the neuroendocrine system by the suprachiasmatic system in the hypothalamus with the adipose tissue and liver in the periphery [8]. The apelinergic pathway is linked to NO balance between the brain, adipose tissue and liver [10] with dietary composition (low calorie diets) and reduction of stress [8] essential to maintain the NO co-ordination of the neuroendocrine system between the brain and peripheral tissues. Nutrigenomic diets are now essential to activate Sirt 1 [11] involved in NO regulation that activates the adipose tissue-liver interaction for the prevention of NAFLD. The crosstalk between the adipose tissue and liver has become of major concern in various communities with adipocyte dysfunction linked to the acceleration of NAFLD [12]. Drugs that lower fat absorption and activate adipose tissue and liver Sirt 1 have been recommended for human use [13] but the use of other anti-obese drugs have raised concerns [14].

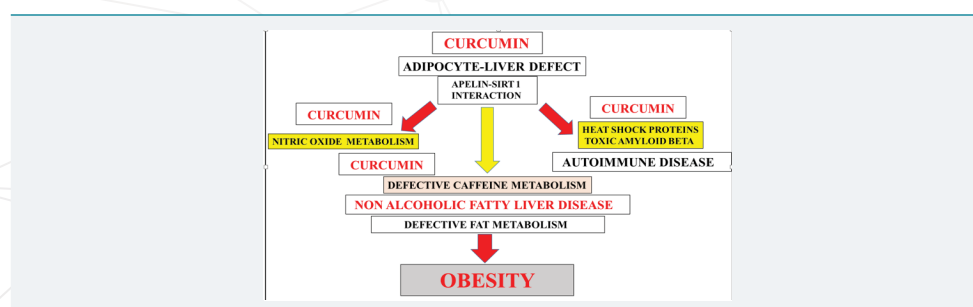
The composition of diets have now become important with adipogenesis a major disorder connected to NAFLD. The reports of obesity to become a pandemic is now related to accelerated aging with mitophagy [15] the major defect in NAFLD. The adipocyte and its transformation with relevance to apelin-Sirt 1 defects is related to autoimmune disease and linked to mitophagy and NAFLD [9,15-17].

Sirt 1 via peroxisome proliferator-activated receptor gamma coactivator 1-alpha releases apelin [18] with Sirt 1/ peroxisome proliferator-activated receptor gamma

coactivator 1-alpha linked to mitochondrial biogenesis [11]. Sirt 1 mutations have been reported in obesity, diabetes, cardiovascular disease and autoimmune disease [2,19-21]. Sirt 1 is the heat shock gene [22,23] with its repression involved with dysregulation of heat shock protein 70 (HSP70), natural killer cell activation and mitophagy [24]. Defective adipose tissue-liver interaction has been treated with caffeine to prevent mitophagy [25,26] linked to adipocyte dysfunction and reversal of NAFLD [27]. Nutrition therapy that allows co-ordination between the brain, adipose tissue and liver activates the apelinergic-Sirt 1 interaction essential for hepatic caffeine metabolism and caffeine's critical role as modulation of Sirt 1 in the brain [28] important to the prevention of obesity.

The health promoting benefits and protective role of Indian spices [29] have been reported in obesity and NAFLD with their role as an antioxidant and antimicrobial agent important to the maintenance of the adipose tissue-liver interaction. Identification of spices such as five commonly used dietary spices include saffron, curcumin, pepper family, zingiber and cinnamon to inhibit amyloid beta aggregation. The curry spice curcumin has been extensively studied in animal models to reduce amyloid pathology with beneficial effects on the prevention of neurodegeneration in man. Curcumin (Figure 1) has been used in various studies to inhibit adipogenesis and decrease adipose tissue mass [30-33]. In the liver curcumin has been shown to stabilize or reverse NAFLD [34-36] but in specific controls curcumin has been shown to increase liver enzymes in short term studies. Indian spices now as novel therapeutic agents are potent in scavenging of NO [37] with relevance to apelin-Sirt 1 neuroendocrine regulation of NO balance. Curcumin has potent effects on NO synthase [38,39] with regulation of Sirt 1 control of NO synthase in endothelial cell in the liver and heart [8] (Figure 1). Curcumin is a potent inducer of the heat shock response [40,41] with complete interference of the heat shock gene Sirt 1 regulation of HSP 70. Low dose curcumin ingestion is indicated with other Indian spice consumption and their clearance from the body is poorly understood [29] with higher dose curcumin involved with increased HSPs associated with amyloid beta aggregation (Figure 1) induced toxicity [40-42].

Cinnamon has now been reported to activate the adipose tissue-liver interaction with cinnamon effects on increased adipocyte lipid and glucose metabolism [43-45]. In the liver cinnamon has been used to stabilize NAFLD [46-48] with its important role as a Sirt 1 activator [29] connected to insulin therapy [49] and its maintenance of the adipose-tissue liver interaction. Consumption of spice intake and its quantification (mg/day) in man [29] vary considerably between countries with cinnamon Sirt 1 activation related to curcumin content with higher doses of curcumin relevant as a Sirt 1 inhibitor. Consumption of Indian spices need to be carefully controlled to avoid induction of obesity by complete nullification of caffeine's co-ordination of the neuroendocrine system by dysregulation of the brain, adipose tissue and liver interaction. Caffeine and its metabolism is critical to cardiovascular disease [50-52] with Indian spice intake (mg/day) now important with relevance to



**Figure 1:** Appetite control is critical to endocrinology and metabolism with apelin-Sirt 1 interaction connected to the adipose-tissue interaction. Endocrine therapeutics that involve the apelin-Sirt 1 interaction and mitochondrial biogenesis are essential to reverse adipocyte dysfunction and the induction of NAFLD. Caffeine and Indian spices are involved with reversal of adipocyte dysfunction and NAFLD. Curcumin at higher doses should be carefully controlled to avoid NO imbalance connected to elevate HSPs with induction of autoimmune and chronic diseases.

interference with caffeine's therapeutic properties in man and various species. Delayed caffeine clearance leads to interference with caffeine's beneficial effect on adipogenesis with increased transport to the brain relevant to mitochondrial induced apoptosis and the induction of Type 3 diabetes [26-28].

## Conclusion

The global obesity epidemic that now affects many countries in the world has not improved in spite of dietary restriction, anti-obese foods and increased physical activity. The neuroendocrine system in many obese individuals is defective with an adipose tissue-liver defect that induces NAFLD and cardiovascular disease. Appetite control to reverse NAFLD and obesity has not been successful with revision of dietary composition that may allow activation of the adipose tissue-liver interaction. Indian spices are important to the adipose-tissue interaction but Indian spice intake should be carefully controlled to avoid curcumin toxicity (apelin-Sirt 1 inhibition) associated with defective fat and caffeine metabolism and associated with the induction of autoimmune and neuroendocrine disease.

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