



# Indian Spices and Unhealthy Diets interfere with Drug Therapy in Diabetes and Neurodegenerative Diseases



Ian James Martins<sup>1\*</sup>

<sup>1</sup>Centre of Excellence in Alzheimer's disease Research and Care, Edith Cowan University, Australia

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**\*Corresponding author:** Ian Martins, School of Medical Sciences, Edith Cowan University, Western Australia 6009, Australia, Tel: 61863042574; Email: i.martins@ecu.edu.au

## Abstract

Nutritional therapy has become important to drug metabolism and treatment with the calorie sensitive gene Sirtuin 1 (Sirt 1) shown to be critical to the prevention of non alcoholic fatty liver disease (NAFLD) with the activation of hepatic drug metabolism. Indian spices have been used extensively in healthy diets in the developing and developed countries for the prevention of NAFLD, diabetes and Alzheimer's disease. Experimental evidence with relevance to ingestion of Indian spices (mg/day) is limited in various countries. Curcumin intake (mg/day) an amyloid beta aggregation inhibitor for the treatment of Alzheimer's disease should be carefully controlled to prevent mitophagy and NAFLD. Indian spices that contain Sirt 1 activators such as cinnamon should be consumed to maintain hepatic drug and spice metabolism with the prevention of insulin resistance. Excessive intake of various Indian spices should be avoided to maintain the therapeutic properties of curcumin and cinnamon and to prevent spice-drug or drug-drug interactions. Data on safety and toxicity of Indian spices may indicate that toxic curcumin effects may be related to over ingestion of various Indian spices relevant to drug induced mitochondrial toxicity in NAFLD, diabetes and neurodegenerative diseases.

**Keywords:** Indian; Spices; Drug; Curcumin; Amyloid Beta; Metabolism; Cinnamon; Sirtuin ; Nutritional Therapy; Nafld; Diabetes; Alzheimer's Disease; Mitophagy; Bacterial Lipopolysaccharides

## Editorial

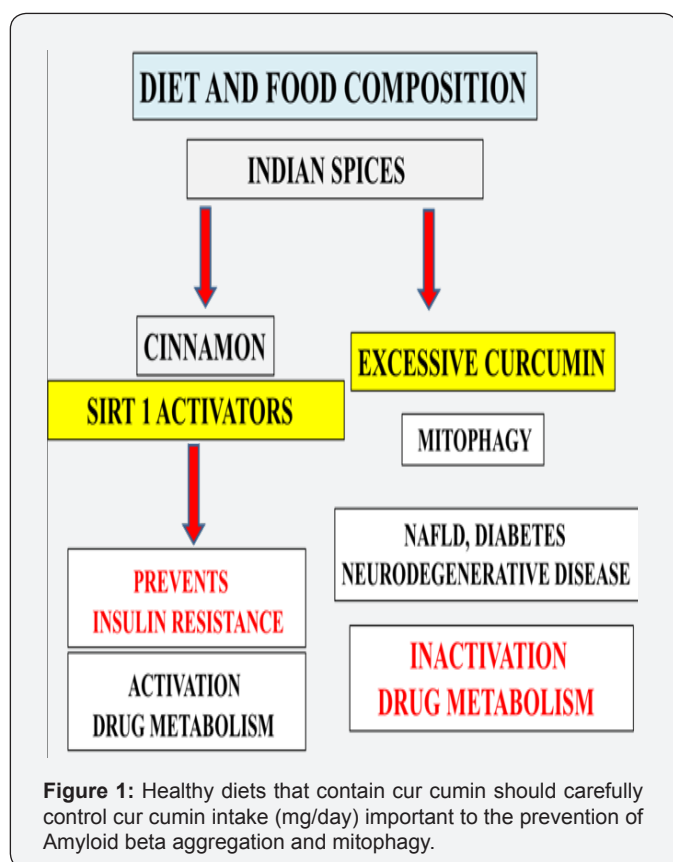
Healthy diets have been encouraged to reverse non alcoholic fatty liver disease (NAFLD) and accelerate hepatic drug metabolism [1] in chronic disease. Genomic medicine and nutrition have become important to drug therapy with the calorie sensitive gene Sirtuin 1 (Sirt 1) shown to be critical to the prevention of NAFLD and activation of hepatic drug metabolism [2-4]. Sirt 1 is a nicotinamide adenine dinucleotide (NAD<sup>+</sup>) dependent class III histone deacetylase (HDAC) that targets transcription factors such as p53 to adapt gene expression to metabolic activity and the deactivation of nuclear receptors indicate its critical involvement in insulin resistance [3]. Appetite control is essential to Sirt 1 and the maintenance of mitochondrial biogenesis [5] for active hepatic fat and drug metabolism [1]. Unhealthy diets that contain bacterial lipopolysaccharides (LPS) repress the anti-aging gene Sirt 1 [6] with relevance to mitophagy and decreased hepatic drug metabolism. Insulin therapy and nutritional therapy [7] are connected to the treatment of NAFLD with a healthy diet in diabetic individuals

essential to prevent NAFLD and chronic disease. The health promoting benefits and protective role of Indian spices has been reported in chronic disease [8] with their role as an antioxidant and antimicrobial agent important to the prevention of NAFLD, heart disease, diabetes and Alzheimer's disease [9-14].

Consumption of spices is higher in countries such as India, China, and Thailand and there has been increased intake of Indian spices in developed countries [8]. Spice intake and its quantification (mg/day) in man has become important with the composition of spices (LPS, xenobiotics) important for risk assessment [9,15-17]. The intake of spices has been shown to vary between different countries and the geographic regions in the same country [8]. Healthy diets that activate fat and drug metabolism are important to hepatic spice metabolism with Sirt 1 activators [18] essential to maintain hepatic Indian spice metabolism and antimicrobial activation [19-21]. The metabolism of various spices from the blood plasma is poorly understood and experimental research needs to be conducted to

determine the amount of Indian spice intake (mg/day) to prevent spice-drug interactions that may interfere with drug therapy in NAFLD and diabetes. Indian spices have been used extensively in healthy diets in the developing and developed countries for the prevention of AD. Identification of spices such as five commonly used dietary spices include saffron, curcumin, pepper family, zingiber and cinnamon [13] to inhibit amyloid beta aggregation. The curry spice curcumin has been extensively studied in animal models to reduce amyloid pathology [22] with beneficial effects on the prevention of neuro degeneration in man [23].

Information regarding curcumin bioavailability and safety in man is lacking with excessive doses associated with nausea, diarrhea, increased risk of bleeding, liver dysfunction (drug metabolism inactivation), hyperactive gallbladder contractions, hypotension (lowered blood pressure), uterine contractions/increased menstrual flow. In the liver mitochondria play a key role in fat metabolism with Sirt 1 connected to mitochondrial biogenesis, drug metabolism and the prevention of NAFLD [1-7]. Curcumin is an important target for mitochondria [24] with elevated curcumin doses associated with interference with mitochondrial DNA [25] and curcumin induced cell death (Figure 1). Data on safety and toxicity of Indian spices may indicate that toxic curcumin effects may be related to ingestion of other Indian spices [8-10,12] relevant to drug-drug interactions and mitochondrial toxicity [26].



Avasimibe is a Sirt 1 activator [27] and may reduce lipophilic curcumin absorption into the blood plasma and delay its rapid sequestration by the mitochondria in various cells [28] with relevance to the months/years of curcumin consumption. Diets that contain Sirt 1 activators such as cinnamon may be important to prevent insulin resistance and maintain drug therapy and hepatic drug metabolism. In vitro and in vivo evidence suggests that cinnamon has anti-inflammatory, antimicrobial, antioxidant, immunomodulatory effects and various other health benefits [29]. Cinnamon has been reported to act as an insulin mimetic and to potentiate insulin activity. Furthermore, animal studies have demonstrated strong hypoglycemic properties. However, there are few controlled clinical studies that can be made about the potential health benefits of cinnamon in humans. Cinnamon is now being reported as a Sirt 1 activator [29,30] with its role in activation of Sirt 1 hepatic amyloid beta and drug metabolism [1].

Sirt 1 has now been reported to be the heat shock gene with its role important to heat shock protein 70 (HSP70) metabolism relevant to the inactivation of amyloid beta metabolism [31-34]. Curcumin as an Indian spice is important to prevent amyloid beta aggregation but not the HSP70 and amyloid beta interaction that is relevant to endoplasmic reticulum stress with relevance to drug toxicity [34,35]. Caffeine is a Sirt 1 modulator and important with relevance to hepatic drug metabolism [36,37] and brain regulation of amyloid beta metabolism relevant to Alzheimer's disease and neurodegenerative disease [1]. Indian spice consumption (mg/day) over years should be carefully calculated to prevent interference with caffeine Sirt 1 modulation with relevance to the rapid brain to liver amyloid beta transport [37]. Information with relevance to Indian spice transport to cells in the brain with relevance to overingestion or defective blood plasma spice metabolism is not available with excessive Indian spice contents in the brain relevant to amyloid beta aggregation and mitophagy.

## Conclusion

Experimental evidence with relevance to ingestion of Indian spices (mg/day) is limited in various countries. Dietary fat may determine curcumin intake (mg/day) (amyloid beta aggregation inhibitor) for the prevention of mitophagy, NAFLD and the treatment of Alzheimer's disease. Sirt 1 activators should be consumed to maintain hepatic fat, curcumin and drug metabolism with the prevention of insulin resistance. Excessive intake of various Indian spices should be avoided to maintain the therapeutic properties of curcumin and cinnamon and to prevent spice-drug or drug-drug interactions. In vitro and in vivo evidence is required with relevance to the blood plasma/liver clearance rates of Indian spices with relevance to hepatic drug inactivation and drug metabolism.

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