

# Effects of Dietary Herbs and Spices

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## Introduction

Whenever the curiosity of the present day investigator probes into the past and brings to light even fragmentary information on the ingenious methods of our ancestors, it makes a fascinating study.<sup>1</sup> In India, reference to the curative properties of some herbs in the Rigveda ( though very brief) seem to be the earliest records of use of plants in medicine. Far more detailed account is available in the Atharva veda. The period of Rigveda is assumed to be between 3500-1800 B.C. After the Vedas there is no information on the development of this science in India for a period of about 1000 years. Then came the two most important works on the Indian system of medicine, Charak Samhita and Susruta Samhita.<sup>2</sup> India, with its wide climatic conditions and topographical features, is perhaps unrivalled in the world and a wide variety of spices of herbs can be grown with ease. With these factors, naturally the Indian medicinal flora is one of the richest and cosmopolitan one with high therapeutic potentialities.<sup>3</sup> By diligent efforts it is possible to utilize the herbal health, for the utmost advantage to humans.<sup>4,5</sup>

Efforts have been made to locate the herbs, identify and study them by using contemporary technological developments with the prime idea of rediscovering comprehensive utility of our ancient heritage and translate it into the terms of reference and application to the modern paradigm of scientific nutrition and human health.<sup>6</sup> The science of nutrition forms a significant part of the study of preventive medicine. Dietary regulation is an important component of treatment of diabetes mellitus,<sup>7-10</sup> atherosclerosis<sup>11,12</sup> constipation<sup>13-16</sup> and other ailments associated with overweight<sup>17,18</sup> and cancer.<sup>19,20,21</sup>

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Research has been going on all over the world to find a desirable diet with ideal features: the blood sugar should not be raised too high after the diet, glucose tolerance should be improved and favourable lipoprotein levels should be achieved.

Spices are dried parts of aromatic plants usually originating in the tropics. Like herbs they provided the flavours to dishes in the ancient world and were highly prized, and the spice trade between Europe and the East led to many of the great voyages of exploration including the "discovery" of America. As with herbs, a range of spices has been and is used particularly in the Middle and Far East where the plants are indigenous. The spices owe their properties to essential oils and a range of astringent substances. These include many biologically active substances which at higher levels of consumption can exhibit toxicity.<sup>22</sup> Two decades back it was considered that though spices themselves contain significant concentrations of some vitamins,<sup>23</sup> the normal levels of use in foods make their nutritional contribution negligible. However recently encouraging data has been compiled to include spices also as nutrients and "nutraceuticals."<sup>24</sup>

## Biochemistry and Composition of Spices and Spice Metabolites

Many spice components are terpenes and other constituents of essential oils. Terpenes are associated with secretory structures in the plant, such as oil cells, resin ducts, glandular trichomes (a hair-like out growth) or glandular epidermis. Indian cooking includes Tamil, Mohammedan, Hindu and other cultural traditions. Many favourite dishes derive from the Hindu cookery, perhaps because its vegetarian basis needed spices to compensate for the blandness. In Western countries it was the preservative action of spices that was of

prime importance. Meat could be preserved for up to a year without refrigeration by pickling it with cloves, wood smoke and mineral salts.<sup>1</sup> Cured pork and sausage were well spiced, mustard seed and ground mustard were likewise used to prolong the life of perishable meat foods while in India pickling using spices and oil certainly developed into a high art. Spices are even more widely employed in foods cooked everyday where the flavour, taste and colour imparting organoleptic properties are of primary concern. In fact the distinguishing characteristics of the numerous regional styles of cooking in our vast country lie very little in the basic food materials employed which are rice, wheat, pulses, vegetables and tubers.<sup>25-27</sup>

### Dietary Spices: The New Nutrients

Since spices, condiments and herbs are consumed in very small quantities every day, their contribution by way of the macroelements of nutrition, namely carbohydrates, proteins and fats, cannot obviously be of any significance. Occasionally however an exceptionally high value of a mineral or even more so of a vitamin, which are two micronutrient groups, could have some meaning in nutrition. This is especially true if the material used is one which is used in fair amount in cooking. The core of classical nutrition research has been to identify and characterise food compounds as nutrients. Many of the non-nutrient compounds have been ignored because they seem biologically inert. However it is becoming apparent that some of these compounds can have rather profound effects in cancer prevention.<sup>19</sup> The future of nutrition research will now require identification of new nutrients which maintain human health by their antioxidative and chemopreventive activity.<sup>24,28</sup>

Dietary spices therefore ought to be classified now as the new nutrients because of their putative health promotive benefits. Tradition attaches all manner of benefit to

every spice, condiment and herb, and they are important ingredients in pharmacopoeias of the Indian system of medicine including Ayurvedic, Siddha and Unani systems.<sup>2,27,29,30</sup>

### Spices and Physiology: Current Research

Spices affect many body functions, from stimulation of chemosenses via their taste, aroma and pungency to their actions on surface membranes, skin and mucosae to their actions on varied systems such as cardiovascular, respiratory, autonomic, metabolic and physiological effects. Research on spices and spice constituents traverses the whole gamut from the molecular and subcellular level through cellular, autocrine, paracrine and endocrine mechanisms to their role in neuro modulation, immunomodulation, anti inflammatory, antioxidant, anticarcinogenic, antimutagenic and psychoactive phenomena. Some of the salient evidences regarding their role are cited herewith.

### General Effects

In the mouth spices exert a mildly irritating action, increasing the flow of saliva, flushing and enhancing digestion. The antiseptic qualities of most spices clear the mouth of bacteria and keep the teeth clean. Their astringent action also helps in maintenance of oral hygiene.<sup>30</sup> In the stomach the carminative actions of spices in expelling gases and relieving distention has been traced to weak closure of the esophageal valve and relaxation of sphincter. Spices are mild stimulants of the heart and perhaps of the lungs, considering that many are quite obviously exhaled in the breath. Nutmeg (jaiphal) and Saffron (zafran) has been shown to enhance the activity of protein digesting enzymes in the body. Allicin present in garlic has a killing action against a wide variety of bacteria and markedly reduces the actual bacterial load in experimental animals. It is also active against fungi. Curcumin, the yellow colouring matter of

turmeric (haldi) has likewise a powerful antibacterial action and asafoetida destroys coliforms and anaerobes in the cecum.

Similarly the suppressive power of many other spice oils has been proven, such as those of ajowain, aniseed (saunf), asafoetida (hing), clove, cinnamon, onion and pepper even against dangerous organisms of the E coli group. In the body, such antibacterial action could help to reduce the flora in the large intestine, thus reducing gas formation.<sup>31</sup> The antiseptic properties of spices also lend them a preservative value when used in foods. Mustard seed and mustard oil perform in this way in Indian pickles, and cloves and cinnamom in murabbas and fruit preserves. The curcumin of turmeric is an antioxidant that can prevent the food from oxidative spoilage, a very common occurrence if an oil is present. A material present in betel leaf called chavicol. Microbes are more easily destroyed in an acidic environment and the various souring agents used in foods like tamarind, kokam and anardhana, could assist in this way. Kokam has been shown to extend remarkably the keeping quality of fresh fish and garlic that of pork.

Turmeric volatile oil markedly reduced the secretion of hydrochloric acid in the stomach. Curcumin (from turmeric) lowered the levels of blood and liver cholesterol and had shown indication of being of value in the management of diabetes. Garlic has been shown to be of therapeutic use in treating the neurological effects of leprosy, perhaps by assisting in the transport of the B vitamin thiamine, across cell membranes. Garlic has also been demonstrated to reduce hypertension in human subjects and to reduce the level of cholesterol in circulating blood.<sup>32</sup>

Capsicum (the globe chilly) has a beneficial effect on peptic ulcers in both healing them and suppressing their formation.<sup>33</sup> Onions, whether raw, boiled or fried, increase the blood fibrinolytic activity. Clove oil has been shown to act on the central

nervous system. Asafoetida has a sedative effect.<sup>32</sup> Caraway oil expels hookworms and is effective against scabies of the skin. However, undesirable effects have also been reported for certain spices. Consumption of safrole, a major constituent in the oils of the leaves of star anise (anasphal) and sassafras (an aromatic root), and a minor one in those of nutmeg (javatri) and cinnamon leaf leads to liver changes that are suggestive of toxicity.

Nutmeg (javatri) and mace (jaiphal) both parts of the same fruit and containing myristicin as a major component in small doses lead to nausea, constipation and stupor. Use of a teaspoonful of either causes fits and hallucinations by disordering the mind.<sup>34</sup> Mustard seed and mustard oil owe their pungency to organic isothiocyanates, which are known to induce goitre, especially when the food is deficient in iodine. A similar goitrogenic effect was even noted for volatile oils from the onion and garlic. Quite a few spice oils are irritating enough to the skin to cause dermatitis, such as those of cinnamon and clove.<sup>35</sup>

### Growth and Development

Nopanitaya claimed that rats fed with a low protein diet supplemented with capsaicin showed the poorest fat absorption and grew at the slowest rate.<sup>36</sup> According to him, capsaicin intake may lead to malnutrition and slow growth in the rats. Caloric intake adjustment at high and at low temperatures has been found to be disturbed in capsaicin desensitized rats. It was concluded that hypothalamic thermoreceptors implicated in both thermoreception and food intake behaviour could be partially damaged by capsaicin. Mahapatra et al. have observed that the weight gain in rats fed with garam masala was less as compared to the control group although the animals were consuming similar quantities of diet.<sup>37</sup> Garam masala when consumed for a period of four weeks decreased the length and weight of the intes-

tine in weanling rats.<sup>38</sup> The entire length of intestine may not be required for the complete absorption, but may shift the site of absorption from one place to another. A higher metabolic rate and respiratory quotient (RQ) on intake of Chinese condiments has been reported.<sup>39</sup>

### Effect on Liver and Intermediary Metabolism

The current paradigm in the research of indigenous medicinal herbs and spices is based on *in vitro* testing, animal models and clinical trials focussed on a group of patients with a common allopathic diagnosis. Most of these plant products have a broad spectrum of activity on the cardiovascular and nervous systems, gastrointestinal tract, liver and related metabolic organs. A wide variety of herbs and their active principles have undergone experimental studies in disease models of liver injury and cholestasis to elicit and establish their hepatoprotective effect.

Curcumin and capsaicin alter bile salt secretion to make it less lithogenic<sup>40</sup> and they also lower cholesterol levels.<sup>41</sup> There is no significant effect on fat absorption.<sup>42</sup> Pepper *asafoetida* and aloe,<sup>43</sup> *Ocimum* (Tulsi),<sup>44</sup> and Eugenol from *Jamun*<sup>45</sup> are hypoglycaemic and antidiabetic agents. The stimulatory effect of capsaicin on serum insulin may be via capsaicin-induced beta adrenergic activity on B cells receptors in pancreatic islets.<sup>46</sup>

Hepatic drug microsomal oxidation appears to be an energy wasteful process because it has no known link with energy conserving mechanisms such as synthesis of ATP and in addition it requires uncoupled oxidation of NADPH. This can appreciably alter the energy balance of the whole body under certain conditions. Such an imbalance would be favoured by repeated intake of drugs that induce hepatic microsomal enzymes. This hypothesis could also be applicable to long term intake of dietary spices and there are studies which point towards the alterations in levels of hepatic

enzymes in response to intake of spices and also influence on basal metabolic rate.<sup>46,47</sup> Liver microsomal cytochrome p-450 dependent aryl hydroxylase has been shown to be generally stimulated by spices. Cummin also stimulates N-demythelase. Singh and Rao have assessed the chemopreventive role of garam masala through its impact on hepatic levels of detoxication enzymes like glutathione-S-Transferase, cytochrome b-5 and cytochrome p-450.<sup>28</sup> They have reported that dietary doses of garam masala modulate the hepatic levels of these enzymes.<sup>28,48</sup> Batra et al. have noted in their observations that 5% garam masala when consumed along with normal diet for a period of four weeks decreases weight of liver significantly.<sup>38</sup> Since liver is the chief organ of metabolism there may be a change in the metabolic status of animals.<sup>49</sup>

### Lipid Metabolism

Several active ingredients of spices including capsaicin (red pepper) piperine (black pepper), curcumin (turmeric), eugenol (clove), ferulic acid (turmeric) and myristic acid (mace amla) influence lipid metabolism predominantly by mobilisation of fatty acids.<sup>42,50,51</sup> Capsaicin is a lipotrope, prevents triglycerides accumulation and increases preferential utilization of fats.<sup>49</sup> Capsaicin stimulates lipid mobilization and lowers perirenal adipose tissue weight and serum triglycerides in fat fed rats.<sup>46</sup> Curcumin, Eugenol and Ferulic acid reduce fatty acid biosynthesis in rat liver and increase skeletal muscle lipoprotein lipase activity.<sup>50,52</sup> Scientists from Central Food Technology Research Institute, Mysore, India have also reported that capsaicin inhibits calcium and calmodulin dependent phosphodiesterase activity in rat adipose tissue which is consistent with adrenaline releasing action of capsaicin reported earlier.<sup>46,53,55</sup> Embelic acid and turmeric are potential hypolipidemic and hypocholesterolemic agents.<sup>42,50</sup>

### Effect on Oxygen Consumption

Capsaicin initially increases oxygen consumption and respiratory quotient followed by a decrease in both before the levels returned to normal, resulting in an overall enhancement of energy metabolism. The effect seen is direct as well as via adrenalin release from adrenal medulla.<sup>46</sup> According to Eldershaw crude extracts of both fresh and dry ginger induce the perfused hind limb to consume more oxygen in association with increase in perfusion pressure and lactate production.<sup>56</sup> The principles responsible for these observations, the gingerol homologues possessed greater motor potency than their shogaol counterparts. Thermogenesis in this study was at least partly, associated with vasoconstriction.<sup>56</sup> Capsaicin has been reported to induce hypothermia as well as release of catecholamines from adrenal medulla.<sup>57</sup> Previous studies in our department by Mahapatra et al have shown that the rats consuming diet containing garam masala spent more time in locomotion, moved a greater distance and had more average speed as compared to control animals.<sup>37</sup> A single bolus of spice does not change thermic effect of feeding acutely but spices have a modulatory role after long term intake.<sup>39</sup> Long term intake of dietary spices (garam masala and coriander) may influence the behavioural changes more than metabolic changes.

### Autonomic Effects

Green chillies cause gustatory sweating associated with lacrimation, salivation and flushing of the face.<sup>58</sup> The distribution of sweating was the same as thermal sweating. On acute administration, both peripherally and centrally, capsaicin produces hypothermia and vasodilation via stimulation of hypothalamic temperature sensitive neurons whereas chronic or intracerebral injection leads to a desensitization, impairment of heat dissipating mechanism and loss of behavioural thermoregulatory

responses to high ambient temperature.<sup>57,59</sup> Capsaicin has potent hypotensive effects on intravenous administration and a pressor response on intracarotid injection.<sup>60</sup> It sensitizes aortic baroreceptors via vagus nerve.<sup>59</sup> It also participates in gastro cardiovascular reflexes.<sup>57,61</sup>

Piperine (black pepper) and capsaicin showed positive inotropic and chronotropic effects in isolated rat atria and exhibited cross tachyphylaxis.<sup>62</sup> Airway reactivity is initially increased by capsaicin followed by desensitization.<sup>63</sup> The respiratory effects of capsaicin vary from apnoea to tachypnoea depending on route of administration.<sup>64</sup> Aloes, garlic, onion and ginger are also beneficial in improving the symptoms of asthma. Ginger root is a putative agent for preventing ageing dependent penile vascular changes and impotence.<sup>65</sup> The mechanism of action of ginger in reducing nausea and vomiting is unknown but it is speculated that it probably works regionally on the gastro intestinal tract rather than on the central nervous system. It may increase gastric motility and absorb neutralising toxins and acids affectively blocking GI reactions and subsequent nausea feedback with no reported side effect. Similarities between cardiovascular responses to food ingestion and to gastric intra-arterial capsaicin ingestion suggested that the compound was stimulating gastric distension receptors.<sup>66</sup> It is also found that the splanchnic nerve itself contains capsaicin sensitive neurons which can mediate cardiovascular effects. South and Ritter made the interesting observation that injections of capsaicin into the area postrema and adjacent nucleus tractus solitarius of the rat resulted in overconsumption of preferred foods.<sup>67</sup> Even more striking with capsaicin treatment was the absence of additional deficiencies that accompany the electrolytic lesions of the same brain stem regions, e.g. chronic body weight loss, excessive angiotensin II induced drinking and diminished food consump-

tion in response to glucose deprivations.<sup>57,68</sup> These observations suggest that capsaicin sensitive afferents in brain stem are critically important to the satiety response. Some of the more recent studies of capsaicin's effects on sensory neurone effects on sensory neurone indicated that systemic administration of the compound increased response thresholds to heat in the rat tail flick and hot plate assays, two classical tests for analgesia in rodents. Systemic capsaicin markedly reduces sensitivity to chemical irritants and also to nociceptive pressure. Capsaicin treatment reduces neurogenic plasma extravasation and vasodilation produces long lasting reduction in systemic arterial pressure, and reduces morphine analgesia.<sup>57</sup>

Buck and Burks also had observed that substance P is absent in the dorsal horn of the spinal cord in victims of familial dysautonomia in which there is a loss of neurons in certain autonomic ganglia and in the dorsal root ganglion. The signs of disease include severe autonomic instability and a marked loss of temperature and pain sensitivity. These observations suggest that animals treated with capsaicin can provide a laboratory model to study aspects of dysautonomia.<sup>57</sup> There are capsaicin sensitive afferents throughout the periphery, involved in monitoring the chemical milieu in the innervated regions and in detecting and signalling functional abnormalities of the CNS extending from skin (e.g. pain and inflammation) to the visceral organs (pain from mucosal ulceration to intestinal muscle dysfunction). That most of these capsaicin sensitive afferents are naturally chemosensitive could indicate that capsaicin is chemically similar to a natural pain producing substance.<sup>69</sup> Search for endogenous receptors for various congeners of spice molecules has yielded encouraging results.

### Future Directions

From the above discussion one can see the emergence of a concept of utility of spices especially towards improvement

in glucose tolerance, blood flow, lipid profile, gastro-intestinal transit, autonomic dysfunction, neural stimulation, anti-oxidative and chemopreventive effects. Most of the work has been done on animal models which were not physiological. Reports from studies on rats who were "hypertensive" or "ethanol pretreated," streptozotocin diabetic, aflatoxin induced carcinomatous, leads us to direct future research perspectives by targeting study of sensitive and labile populations like "hypertensives," "diabetics," "hyperlipidaemics," "dysautonomics" or Reaven's metabolic syndrome X patients.

Today when the world, including our country India, is undergoing an epidemiologic shift towards non-communicable diseases, we do need to answer questions on whether prescriptions of certain select spices according to our eminent heritage is beneficial in this context. Controlled clinical trials including blinded trials and meta-analyses of observed effects need to be done to clearly and unequivocally resolve this issue. Today when the world all over is going 'green' we again need to channel our resources and research skills to formulate studies which clearly elucidate and elaborate the normal physiological role of these natural staple food additives used in our traditional cooking and accord them their due as proactive, promotive and prescriptive nutrients.<sup>24,69-72</sup>

### References

1. Clair C : *Of Herbs and Spices*. London: Abelard-Schuman, 1961; 1-16.
2. *Charaka: Charak Samhita, Sutra Sthan. Varanasi*. Chaukamba Surbharati Prakashan. 1994; 18,32,353.
3. Council of Scientific and Industrial Research: Wealth of India-Raw Material. *CSIR Publication*. 1976; 78.
4. Akerele O: Nature's medicinal bounty: don't throw it away. *World Health Forum*, 1993; 14(4): 390-395.
5. Bhupat R : Use of Indian ethnic remedies (letter) *Br Med J*, 1993; 306 (6883): 1003-1004.
6. Cox PA : The ethnobotanical approaches to drug

- discovery. Strengths and limitations. *Ciba Found Symp*, 1994; 185: 25-36.
7. Wolever TMS, Nutall FQ, Lee R : Prediction of the relative blood glucose response of mixed meals using white bread glycaemic index. *Diabetes Care*, 1985; 8: 418-28.
  8. Wolever TMS, Nguyen PM, Chiasson JL, et al : Determinants of GI calculated retrospectively from diet records of 342 individuals with NIDDM. *Am J Clin Nutr*, 1994; 59(6).
  9. Jenkins DJA, Wolever TMS, Jenkins AL : *Modern Nutrition in Health & Disease*. Philadelphia. Lea & Febiger. 1994; 583-602.
  10. Anderson JW, Geil PB : *Modern Nutrition in Health and Disease*. Philadelphia. Lea & Febiger. 1994; 1259-86.
  11. Abrams ME, Jarett RJ, Keen H, Boyns DR, Corsslay JN : Oral glucose tolerance and related factors in a normal population Sample II, interrelationships of glycerides, cholesterol and other factors with glucose and insulin response. *Br Med J*, 1969; 1: 599-602.
  12. Chait A, Brunzell JD, Denke M A et al : Rationale of the Diet. Heart statement of the American Heart Association Report of the Nutrition Committee. *Circulation*, 1993; 88(6): 3008-3029.
  13. Kurpad AV, Shetty PS : Methods for the estimation of intestinal transit time in the tropics. *Trop Gastroenterol*, 1985; 6: 197-202.
  14. Welch MCL, Read NW : Regulation of gastrointestinal function by ileal nutrients in health and disease. *Trop Gastroenterol*, 1986; 116-125.
  15. Horowitz M, Wishart J, Medolox A, Russo A : The effect of chilli on gastro intestinal transit. *J Gastroenterol Hepatol*, 1992; 7(1) : 526.
  16. Holzer HH, Turkelson CM, Solomon TE, Raybould HE : Intestinal lipid inhibits gastric emptying via CCK and a vagal capsaicin sensitive afferent pathway in rats. *Am J Physiol*, 1994; 67(4 tp 1): G625-629.
  17. Jung RT, Shetty PS, Barrant M, Callingham BA, James WPT : Role of catecholamines in hypotensive response to dieting. *Br Med J*, 1979; 1: 12-3.
  18. Willett WC : Diet and health. What should we eat? *Science*, 1994; 264(5158): 532-537.
  19. Wattenburg LW : Inhibition of Neoplasia by minor dietary constituents. *Cancer Res Supply*, 1983; 43: 2448s-2453s.
  20. Kohlmeier L, Simonsen N, Mottus K : Dietary modifiers of Carcinogenesis. *Environ Health Perspect*, 1995; 103(suppl 8): 177-184.
  21. Stich HF, Rosin MJ : *Nutritional and Toxicological Aspects of Food Safety*. New York. Plenum Press. 1984; 1-24.
  22. Southgate DAT : *Spices and Beverages In Essential Human Nutrition and Dietetics*. Edinburgh. Churchill Livingstone. 1993; 325-34.
  23. *US Department of Agriculture : Composition of foods. Hand Book No.8 revision, 8-2 Spices and Herbs*. US Government Printing Office, Washington. 1977.
  24. Hendrich S, Lee K-W, Xu X, Wang HJ, Murphy PA : Defining food components as new nutrients. *J Nutr*, 1994; 124(9 Suppl): 1789s-1792s.
  25. Gopalan C, Ramasastri BV, Balasubramaniam SC : *Nutritive value of Indian Foods*. National Institute of Nutrition Hyderabad, ICMR Publication. 1971; 1-30.
  26. Achaya KT : *Everyday Indian processed foods*. New Delhi. National Book Trust, India, 1986; 74-90.
  27. Pruthi JS : *Spices and condiments*. New Delhi. National Book Trust India. 1987; 5, 41-43, 185-191.
  28. Singh A, Rao AR : Evaluation of the food additive garam masala on hepatic detoxication system. *Indian J Exp Biol*, 1992; 30(12): 1142-1145.
  29. Bhatt NS, Bhat AD : Indigenous drugs and liver disease. *Ind J Gastroenterol*, 1996; 15(2): 63-67.
  30. Hameed HA : *The complete book of home remedies*. New Delhi. Orient Paperbacks. 1982; 39-50.
  31. Bhavanishankar TN, Murthy VS : Inhibitory effect of curcumin on intestinal gas formation by clostridium perfringens. *Nutr Rep Int*, 1985; 32(6): 1285-92.
  32. Bordia A, Bansal HC, Arora SK, Singh SV : Effect of essential oils of garlic and onion on alimentary hyperlipidaemia. *Atherosclerosis*, 1975; 21 : 15-19.
  33. Kumar N, Vij JC, Sarin SK, Anand BS : Do chillies influence healing of duodenal ulcer? *Br Med J*, 1984; 288: 1803-4
  34. Schultes RE, Hofmann A : *The Botany and Chemistry of Hallucinogens*. Springfield Illinois. Thomas. 1980.
  35. Ninimmaki A, Hannuksela M : Immediate skin test reactions to spices. *Allergy*, 1981; 36(7) : 487-493.
  36. Nopanitaya W : Long term effects of capsaicin on fat absorption and growth of the rat. *Growth*, 1973; 37 : 269-279.
  37. Mahapatra SC, Batra V, Singh R, Verma MK, Kochhar KP : Long term intake of dietary spices increases locomotor activity in rats. *Indian J Physiol Pharmacol*, 1992; 36(5 suppl): 36 (Abst).
  38. Batra V, Singh R, Kochhar KP, Mahapatra SC : Effects of dietary spices on gastrointestinal structure and function in rats. *Indian J Physiol Pharmacol*, 1992; 36(5 suppl): 36 (Abst).
  39. Viarouge C, Caulliez R, Nicolaidis S : Umami taste of monosodium glutamate enhances the

- thermic effect of food and affects the respiratory quotient in the rat. *Physiol Behav*, 1992; 52(5) : 879-884.
40. Bhat BG, Srinivasan MR, Chandrashekhara N : Influence of curcumin and capsaicin on composition and secretion of bile-in rats. *J Food Sci Tech*, 1984; 21 : 224-226.
  41. Dixit VP, Jain P, Joshi SC : Hypolipidaemic effects of Curcuma longa L and Nardostachys jatamansi, DC in triton-induced hyperlipidaemic rats. *Indian J Physiol Pharmacol*, 1988; 32 : 299-304.
  42. Srinivasan MR, Satyanarayana MN : Influence of capsaicin, curcumin and ferulic acid in rats fed high fat diets. *J Biosci*, 1987; 12 : 1943.
  43. Al-Awadi FM, Khaltair MA, Gunar KA : On the mechanism of hypoglycaemic effect of a plant extract. *Diabetologia*, 1985; 28(7) : 432-434.
  44. Bhardwaj PK, Dasgupta DJ, Parashar BS, Kaushal SS : Control of hypoglycaemia and hyperlipidaemia by plant product. *J Assoc Phy India*, 1994; 42 : 33-35.
  45. Kohli KR, Singh RH : A clinical trial of Jambu (Eugenia jambolana) in Non-Insulin Dependent Diabetes Mellitus. *JRAS (J Res in Ayurveda and Siddha)*, 1993; XIV(3-4) : 89-97.
  46. Kawada T, Watanabe T, Takaiishi T, Tavaka T, Iwai K : Capsaicin-induced B-adrenergic action on energy metabolism in rats: influence of capsaicin on oxygen consumption, the respiratory quotient, and substrate utilization (42414). *Proc Soc Exp Biol Med*, 1986; 183 : 250-256.
  47. Henry CJ, Emery B : Effect of spiced food on metabolic rate. *Hum Nutr Clin Nutr*; 1986; 40(2): 165-168.
  48. Singh A, Rao AR : Evaluation of the modulatory influence of black pepper (Piper nigrum, L.) on the hepatic intoxication systems. *Cancer Lett* 1993; 72(1-2): 5-9.
  49. Sambaiah K, Satyanarayana MN : Influence of red pepper and capsaicin on body composition and lipogenesis in rats. *J Bio Sci*, 1982a; 4 : 425.
  50. Thakur CP, Thakur B, Singh B, Sinha PK, Sinha SK : The Ayurvedic medicines haritaki, amla and bahera reduce cholesterol-induced atherosclerosis in rabbits. *Int J Cardiol*, 1988; 21 : 167-175.
  51. Kumari MV and Rao AR : Effect of mace (Myristica fragrans. Houtt) on cytosolic glutathione S. transferase activity and acid soluble sulphhydryl level in mouse liver. *Cancer Lett*, 1989; 46(2): 87-91.
  52. Kawada T, Hagihara K-I, Iwai K : Effects of capsaicin on lipid metabolism in rats fed a high fat diet. *J Nutr*; 1986; 116 : 1272-1278.
  53. Sambaiah K, Satyanarayana MN : Stimulation of liver triglyceride secretion in rats by capsaicin. *Curr Sci*, 1987; 56 : 897.
  54. Sambaiah K, Satyanarayana MN : Effect of capsaicin on triglyceride accumulation and secretion in ethanol fed rats. *Ind J Med Res*, 1989; 90 : 154-158.
  55. Salimnath BP, Satyanarayana MN : Inhibition of calcium and calmodulin dependent phosphodiesterase activity in rats by Capsaicin. *Biochem Biophys Res Commun*, 1987; 148-292.
  56. Eldershaw TP, Colquhoun EQ, Dora KA, Peng ZC, Clark MG. Pungent principles of ginger (Zingiber officinale) are thermogenic in perfused rat hind limb. *Int J Obesity*, 1992; 16(10) : 755-763.
  57. Buck SH, Burks TF. The neuropharmacology of capsaicin: recent observations. *Pharmacol Rev*, 1986; 38 : 179-226.
  58. Lee TS. Physiological gustatory sweating in a warm climate. *J Physiol*, 1954; 124 : 528-542.
  59. Virus RM, Gebhart GF. Pharmacological action of capsaicin: Apparent involvement of substance P and serotonin. *Life Sc*, 1979; 25 : 1273-1284.
  60. Virus RM, Kneenpfer MM, McManus DQ, Brody MJ, Gebhart GF. Sensory cardiovascular and neurochemical effects of capsaicin. *Fed Proc*, 1990; 39 : 595.
  61. Martin SE, Pilkington DM, Longhurst JC. Coronary vascular responses to chemical stimulation of abdominal visceral organs. *Am J Physiol*, 1989; 256(3 pt 2) : H735-744.
  62. Miyauchi T, Ishikawa T, Sugishita Y, Saito A, Goto K. Involvement of calcitonin gene related peptide in the positive chronotropic and inotropic effects of piperine and cross tachyphylaxis between piperine and capsaicin in isolated rat atria. *J Pharmacol Exp Ther* , 1989; 248 : 1816-1824.
  63. Lundberg JM, Saria A. Capsaicin induced desensitization of airway mucosa to cigarette smoke, mechanical and chemical irritants. *Nature (Cond.)*, 1983; 302 : 251-253.
  64. Palecek F, Sant'Ambrogio G, Sant'Ambrogio FB, Mathew OP. Reflex responses to capsaicin: intravenous aerosol and intratracheal administration. *J Appl Physiol*, 1989; 67(4): 1428-37.
  65. Backon J. Ginger as an antiemetic : possible side effects due to its thromboxane synthetase activity. *Anaesthesia*, 1991; 46 : 705-6.
  66. Lembeck F. Columbus : Capsicum and capsaicin : past, present and future. *Acta Physiol Hung*, 1987; 69 : 265-273.
  67. South EH, Ritter RC. Over consumption of preferred foods following capsaicin pretreatment of the area postrema and adjacent nucleus of



- the solitary tract. *Brain Res*, 1983; 288 : 243-251.
68. Buck SH, Deshmukh PP, Yamamura HI, Burks TF. Thermal analgesia and substance P depletion induced by capsaicin in guinea pigs. *Neuroscience*, 1984; 6 : 2217-2222.
69. Kumazawa T. Functions of nociceptive Primary Neurones. *Jap J Physiol*, 1990; 40(1) : 1-4.
70. James WPT. Nutrition Science and policy research: Implications for Mediterranean diet. *Am J Clin Nutr*, 1995; 61 (suppl 2): 31-41.
71. Keys A. Mediterranean Diet and Public Health: personal reflections. *Am J Clin Nutr*, 1995; 61(suppl): 1321-1323s.
72. Kochhar KP. *An Experimental Study on some Physiological Effects of Dietary Spices*. Thesis submitted to All India Institute of Medical Sciences in partial fulfilment of requirement for Ph.D. August, 1996.