Spices have been part of the Indian culinary art since ancient times. Turmeric, an Indian spice referred to as ‘Haridara’ in Vedic texts, is used for its colour, flavour and digestive properties. Further, in Ayurveda, the ancient medical practice of the Indian system of medicine, it is documented as a medicinal agent by Charaka and Sushruta. In fact, turmeric is referred to as ‘Indian Saffron’ or ‘Salt of the Orient’. Besides its use as a spice, it finds a place in cosmetics for its brilliant yellow colour and characteristic perfume. It is always used on auspicious and religious occasions, giving it a special place in Indian culture.

Its origin can be traced to South and South-east Asia, where it is grown on the slopes of hills of the tropical forest. India is the largest producer of turmeric. Genus Curcuma belongs to the family Zingiberaceae and consists of many species. The commonly used spice is Curcuma longa Linn, yielding turmeric of commercial value.

It is a herbaceous plant with thick and fleshy rhizomes. The underground rhizome is cured and used as the spice. The turmeric sticks are cured by cooking, when the main component, namely starch granules, gelatinises. The cooking facilitates sundrying and controls the colour and aroma of the final product. The sundried rhizomes are polished either mechanically or manually.

Turmeric is a household spice used in several food preparations. It is used with vegetables, meat, pulses and in spice mixtures. It is one of the basic components of the curry powder which is available in markets all over India. Curry powders are also packed for export.

In the West, turmeric is used in mustard paste and margarine. The use of oleoresin, an extract of turmeric, is becoming increasingly important in the developed countries where the food industry has made phenomenal progress. In this form, it is free from microbial contamination and is therefore readily used in frozen, ready-to-eat and other convenient foods. Earlier, turmeric was also used as a dye for colouring fabrics.

The medical use of turmeric dates back to ancient times. It has been used specifically to treat contusions, bruises, sprains and as a carminative and astringent. Turmeric has antiseptic and vermifugal properties. Its active component curcumin as a medicament has received much attention in recent times in India.

The anti-inflammatory and anti-rheumatic activity has been investigated in depth with positive effects in acute and chronic models of inflammation. Organic extracts of rhizomes show colorectal activity and decrease the cholesterol level in hypercholesterolemic rats. It has some anti-bacterial properties. Its efficacy in asthma is documented.

Chemical Composition

Turmeric is bright yellow to dull yellow in appearance with a rough surface. The chemical composition indicates that it has starch (40-50 per cent), protein (6-10 per cent), fat (5-8 per cent), fibre (3-5 per cent), fixed (7 per cent) and volatile (4 per cent) oils and ash (3-7 per cent).

In addition it has several micro-nutrients such as carotenes, thiamin, riboflavin, niacin, vitamin C, iron, zinc, calcium, magnesium and selenium in varying concentrations.

The yellow colour of turmeric is due to its functional compound curcumin, the yield of which varies from 2-5 per cent. The structure of the curcumin as diferuloylmethane was first suggested in 1917 and confirmed later by synthesis! In addition to curcumin, two other compounds namely demethoxy and bisdemethoxy curcumin are also found in turmeric.

The oleoresins are mixtures of compounds such as volatile oils, non-volatile fatty and resinous materials extractable by solvents. It is a concentration of all constituents contributing to flavour in the original spice. The curcuminoid content in extracted oleoresin is around 45 per cent. The aroma of turmeric is also due to its volatile oils. Turmeric as sticks, powders or oleoresin is stable. The colour is stable only when protected against sunlight.

Anti-cancer Effect

Dietary factors are widely believed to play an important role in determining the risk of several cancers. Dietary practices may increase or decrease cancer risk, depending on the balance of harmful versus beneficial constituents of foods. Many foods contain inhibitors of carcinogenesis which may enhance the body’s natural defence mechanisms against cancer. This brief write-up reviews the various Indian studies on the spice turmeric, for its plausible cancer prevention effects.

The process of carcinogenesis: Carcinogenesis induced by chemicals involves the separate and independent processes of initiation, promotion and progression. The genetic damage, namely, initiation where DNA is damaged, is followed by epigenetic promotional events which through progression manifest as cancer. Initiated cells may lie dormant in the absence of a promotor. Promotors induce multiplication of initiated cells. The slow complex process of promotion may be reversed and progression halted by exogenous factors such as those encountered in the diet.

Numerous mechanisms for inhibition of carcinogenesis have been documented. The inhibitors may reduce conversion of procarcinogen to carcinogen, may induce detoxification of carcinogens, scavenge reactive carcinogen species, induce cellular differentiation and repair, alter cell receptors or reverse any other pre-neoplastic process.

Generally the inhibitors, therefore, are considered as blocking agents which prevent carcinogen from reaching or reacting with critical target cells. Suppressing agents are compounds that inhibit carcinogenesis when administered, subsequent to the course of carcinogen exposure and are termed as anti-promoters. Naturally-occurring dietary constituents can act by any one of these mechanisms.

We will now briefly review the evidence favouring turmeric as an inhibitor of the process of carcinogenesis.
In Vitro Studies

Anti-mutagenicity: Several laboratories in India have been evaluating turmeric as a non-mutagenic and anti-mutagenic agent using the classical Ames test. Extracts of fresh and dried turmeric, its principal component, curcumin, and pyrolysed turmeric powder tested for mutagenicity were found to be negative. On the other hand, these constituents were found to have anti-mutagenic effect against extracts of chilies and capsaicin, both with and without in vitro activation of the compounds by rat liver microsomes. The pyrolysed product of turmeric also did not exhibit any mutagenicity but had anti-mutagenic properties. The oleoresin is non-mutagenic and, in the yeast gene conversion test, has been found to be non-toxic.

When curcumin in a dose-dependent manner was tested against several environmental mutagens such as extracts of beedi, cigarette smoke condensate and tobacco and masheri extracts, benzo(a)pyrene (B(a)P), dimethylbenzanthracene (DMBA), it was evident that curcumin antagonised the mutagenicity of all genotoxins which needed metabolic activation.

These early studies lead one to hypothesise that turmeric and curcumin are potent anti-mutagens which can probably be used to prevent neoplasia. However, one of the major problems of such in vitro tests is that they do not give any indication of whether a compound when fed in the diet is capable of getting across membrane barriers and have similar effects under in vivo situations.

Cytotoxicity: Research on the effects of turmeric and curcumin on cytotoxicity in cultured cells have yielded encouraging results. Water extracts, ethanol extracts and curcumin were tested for cytotoxicity against Chinese Hamster Ovary (CHO) cells in tissue cultures. They inhibited the growth of CHO cells in culture. A concentration of 4 µg/ml of curcumin had a 50 per cent inhibition effect while 10 µg/ml were needed for 100 per cent inhibition.

The cytotoxicity was also determined against Dalton's lymphoma ascitis tumour cells. Alcohol extracts of turmeric were better as compared to water extracts and the quantity of extract of turmeric needed for 50 per cent cytotoxicity was 200 µg. The inhibition was proportional to the amount of curcumin present in various levels of extracts. Curcumin in doses of 8 µg/ml produced 100 per cent cytotoxicity of Dalton's lymphoma ascites tumour cells.

In Vivo Studies

Experimental observations: The anti-mutagenic effects of turmeric were examined against the ubiquitous pollutant B(a)P and 3 methyl cholanthrene (3 MC), an inducer of the microsomal enzyme. Animals were fed various levels of turmeric in the diet ranging from 1-10 per cent for four weeks and were dosed with either B(a)P (1.5 mg) or 3 MC (1.5 mg) by the intraperitoneal route. The urine samples were collected for quantifying the mutagens excreted. The results show that turmeric inhibited B(a)P-induced mutagenesis. The mutagenicity of polycyclic aromatic hydrocarbons occurs mainly after metabolic activation by microsomal mixed function oxidases and epoxide hydrolases. Under conditions of induction, one can expect to have more potent carcinogens formed in vivo. It also had a similar effect even when the mixed function oxidations were induced by 3 MC. More recent findings on curcumin-fed animals (0.016 per cent and 0.03 per cent in the diet) further confirmed that the anti-mutagenic effects of turmeric are due to curcumin.

Studies in humans: Tobacco smoke is one of the important sources of human exposure to mutagens and carcinogens, and it is known that both active and passive smokers excrete a large number of tobacco-derived mutagens in urine. As it is possible to quantify mutagens in urine, the beneficial effects of turmeric administration on urinary excretion of mutagens were investigated, along with the adverse effects, if any, on kidney and liver function in smokers. While the non-smokers had very low levels of urinary mutagens as indicated by the histidine revertants in the Ames assay, the smokers had almost a three-to eight-fold increase in the mutagens excreted.

When such subjects were given turmeric in doses of 1.5 gm/day for 15-30 days, it was evident that it significantly decreased the urinary mutagens by 30-40 per cent with or without activation of mutagens. This dose of turmeric, fed for a period of one month, did not have any effect on either the liver function or the kidney function. Nor did it have any effect on the lipid profile. Turmeric appears to be an excellent agent to counteract the genotoxicity of tobacco-derived mutagens in doses which are easily consumed in the daily diet.

Effect on B(a)P-DNA Adducts

As genotoxicity involves damage to DNA, the effect of turmeric on DNA damage was assessed. Using the 32P post-label assay to quantify B(a)P-DNA adducts, the effects of curcumin/turmeric were evaluated. It was interesting to observe that turmeric fed at levels of 0.1 per cent and 0.5 per cent in the diet had comparable effects to 3 per cent in the diet. It was even more interesting and encouraging to observe that as low as 0.03 per cent of curcumin is more effective (>90 per cent inhibition of DNA adduct formation). Curcumin or B(a)P-DNA interaction studied by radio-labelled B(a)P (H3) on the dorsal skin of mice gave similar results. Dietary substances that interfere with the formation of carcinogen-DNA adducts and decrease the binding of electrophilic substances with critical nucleophilic macromolecules such as DNA are considered to be excellent blocking agents.

Studies of this nature under in vivo situations clearly show that both turmeric and curcumin fed at very low levels in the diets are available to biological action.

Single Strand Breaks

Single strand breaks (SSb) in DNA estimated by alkaline elution assay indicate DNA damage, repair and replication. Saccharomyces cereviciae (yeast) exposed to UV irradiation, 8-methoxypsoralen and B(a)P manifest genotoxic damage in the form of SSb. The SSb formed were reduced by treating the yeast cells with curcumin in vitro. In vivo studies on SSb in the fore-stomach mucosa of mice exposed to B(a)P were found to be much less on curcumin treatment.

Tumour Models

The inhibitory effects of curcumin on tumour promotion in mouse skin induced by 12-0-tetra deonylphorbol 3-acetate (TPA) are documented. Topical applications of 0.5 to 10 µl...
cromoles of curcumin inhibited epidermal ornithine decarboxylase activity, thymidine incorporation into epidermal DNA (29 per cent-49 per cent inhibition) and tumours (100 per cent inhibition) — all induced by DMBA. The effects of curcumin in concentrations of 10 micromoles was found to be superior to that of other phenols such as caffeic, ferulic and chlorgenic acid on TPA-induced tumour promotion in mice skin.

Since oral cancers are more widely prevalent in India, a hamster cheek pouch model was used in our laboratories to study the tumour preventive effects induced by poly cyclic aromatic hydrocarbons DMBA. Small doses such as 1 per cent turmeric in the diet successfully counteracted the tumour. Other studies on DMBA-induced skin carcinogenesis, particularly on papillomas, gave essentially similar results. It was also shown that survival of tumour-bearing animals was prolonged by curcumin treatment as it effectively inhibited tumour formation in mice induced with Dalton’s lymphoma ascitis tumour cells. In an experiment on mutagenesis where the animals were exposed to repeated administrations of B(a)P, several rats developed malignant fibrosarcoma while none of the rats in the 10 per cent curcumin-fed group developed subcutaneous tumours. Despite repeated carcinogen treatment, the 10 per cent curcumin-treated rats did not exhibit any tumours.

Further, turmeric and curcumin have been found to reverse aflatoxin-induced liver damage produced by feeding aflatoxin to ducklings. The fatty changes, necrosis, biliary hyperplasia produced by AFB, were reversed.

**Turmeric/Curcumin Doses**

From the various experimental data presented, particularly the *in vivo* studies, it is evident that turmeric at 0.1 per cent in the diet can decrease mutagenesis, carcinogenesis and DNA damage. The human dose extrapolations based on pharmacological principles of body surface area and metabolism indicate that about 8-10 mg/kg would suffice for an adult man. Therefore, a dose of about 500-1,000 mg of turmeric per day would be adequate to offer protective effects. Its curcumin equivalents are far below the therapeutic doses used for anti-inflammatory effects. Turmeric consumption in India is high, as almost 70 per cent of the produce is being marketed locally. Documented per capita consumption is 0.16-0.44 kg per year per person. A high intake of 0.6 gm per capita per day is reported in rural areas as against 0.2 gm per capita per day in urban India. Hence it would not be difficult to increase the turmeric from its present consumption level to 1-1.5 gm/day in the diet.

**Mechanisms of Action**

**As an anti-oxidant:** As indicated earlier, there are several mechanisms by which one can counteract the effects of carcinogens on the body. Highly reactive oxygen molecules or oxygen radicals generated by carcinogens or their metabolites in the body are trapped by several anti-oxidants. The anti-oxidant properties of curcumin have been demonstrated as early as 1976. In an elegant experiment under *in vitro* situations, liposomal lipid peroxidations and peroxide-induced DNA damage investigated, revealed that curcumin and the water-soluble extracts of turmeric counteracted the damage. Very small concentrations (100 ng/ml) were found to be as effective as butylated hydroxyanisole (BHA) — a potent anti-oxidant.

While studying the mechanisms of the anti-carcinogenic action of turmeric, an aqueous turmeric extract has been recently isolated and characterised. It has been identified as a water-soluble 5-kDa peptide turmerin from turmeric which has anti-oxidant and anti-mutagenic activity. It appears to be a heat-stable, non-cyclic peptide containing 40 amino acid residues, not sensitive to trypsin, pepsin, heat and UV radiation, and non-cytotoxic as tested in Ames assay and in human lymphocytes.

**Turmerin, in indirect experiments, has been shown to decrease arachidonic acid release, which is recognised as an important event in membrane-mediated chromosomal damage. The protective effects of curcumin have been demonstrated in paracetamol-induced hepatocytotoxicity *in vitro* and *in vivo*.**

**Inhibitor of conversion to active carcinogens:** More recent studies ascribe certain other functions to curcumin and turmeric, such as the prevention of nitrosamine formation from precursors such as nitrates and amines. Aflatoxin production has been counteracted by extracts of turmeric.

**As a detoxificant:** Yet another mechanism by which turmeric or curcumin exhibits its protective effects is through detoxification mechanisms. It is now known that turmeric feeding induces glutathione-S-transferase and UDP-glucuronyl transferase activities in the intestines and liver. Glutathione-S-transferases play an important physiological role in the detoxification of potential carcinogens and pharmacologically active compounds. An increase in glutathione-S-transferase is known to inhibit experimentally-induced tumours.

**As a prostaglandin inhibitor:** Curcumin is a potent anti-inflammatory agent. It inhibits arachidonic acid production and results in decreased yield of TPA-dependent tumours. Curcumin is a potent anti-inflammatory agent. It is as potent as phenylbutazone in inflammatory tests in animal species. Curcumin used as an anti-inflammatory agent inhibits platelet cyclo-oxygenase and the release of thromboxane A₂ without inhibiting the generation of PG I₂ and II. Its anti-inflammatory effect may explain its protective effect against DNA damage and promotional aspects of cancer. The above mechanisms suggest that turmeric/curcumin can act as both anti-initiator and promoter.

**Pharmacokinetics of Curcumin**

The uptake, distribution and excretion of turmeric studied in Sprague Dawley rats when curcumin was given by the oral route indicate that curcumin was excreted in faeces while negligible amounts appear in the urine. Synthesised curcumin is poorly absorbed, though when administered by the IV route, curcumin is actively transported into bile. It appears to be actively metabolised in the liver. The metabolism of labelled (¹⁴C) curcumin administered by the parenteral route, showed that the urinary excretion was very low, with radioactivity being distributed in the blood, liver and kidney. It appears to be metabolised to glutathione and sulfate conjugates, which are primarily excreted in the bile. Its half-life in rabbits is around six hours.

**Toxicological aspects of turmeric and curcumin:** An FAO/WHO committee of experts approved turmeric and curcumin as food additives.
with the acceptable daily intake of turmeric as 2.5 mg/kg body weight and that of curcumin as 0.1 mg/kg body weight. Turmeric, in our own studies, fed at levels varying from 1-10 per cent did not exhibit any adverse effects on organs and tissues. Turmeric and curcumin fed at 0.5 per cent and 0.15 per cent, respectively, for 12 weeks did not produce any genetic damage.

Alcoholic extracts of turmeric, fed at 60 mg in rats, monkeys, guinea pigs and dogs for 12-13 weeks, were again negative for toxicity. Pigs fed with turmeric oleoresins for three to four months at 60-150 mg/kg body weight per day levels showed a reduction in weight gain with some epithelial changes in the liver and kidneys. Rats administered curcumin in doses of 400, 800 and 1,600 mg/kg/day for 90 days did not show any change. Growth, behaviour, and biochemical and histological parameters failed to detect any possible toxicity. No evidence of teratogenicity was observed on doses of 800-1,600 mg/kg in mice and 300-600 mg/kg in rabbits. In a double blind clinical study with curcumin in doses of 1,800-2,100 mg/day for five-10 weeks, no side effects were reported.

The doses employed in these above studies are several times greater than the normal consumption by the human population and also than the acceptable daily intakes prescribed by FAO/WHO, while the doses which we are suggesting for the prevention of cancer are far below that required for anti-inflammatory activity.

Though curcumin may be easy to administer as a tablet or a capsule, the possibility of consuming more turmeric in the diet as a natural preventive measure should be considered. One can without much hesitation advise 1-2 gm turmeric to be consumed in the diet every day. This may have the beneficial effect of mitigating the effects of carcinogens.

Comment: Turmeric is sometimes adulterated with lead chromate in order to deepen its yellow colour and increase its appeal to the consumer. This is prohibited under the law. It will be important to ensure that this prohibition is strictly enforced, especially if, because of its beneficial properties discussed above, increased intake of turmeric is to be promoted.

References

FOUNDBATION NEWS

Publication: Special Publication 9, "Towards Better Nutrition — Problems and Policies" edited by C. Gopalan and authored by 44 distinguished scientists (about 450 pp, price: Rs 250) has just been released. There are seven sections in the publication: Community health/nutrition problems; Women and child nutrition; Foods and diets; Energy metabolism; Vitamin A; National nutrition programmes; and Nutrition and Diseases. The editors in each section attempt to delineate the problems and to outline possible strategies for their control. Copies can be obtained from the Nutrition Foundation of India.
Having actively participated in the deliberations leading to the setting up of the Food and Nutrition Board some decades ago, I am aware of the high hopes and expectations with which the Board had been set up. In its early years, it had carried out commendable work. With progressive tightening of the bureaucratic stranglehold in recent years, the Board’s stature and efficacy had become somewhat eroded — a situation that must have caused considerable frustration to the scientists functioning in it.

Now, with the formulation of the ‘National Nutrition Policy’, the Board has been “shifted” lock, stock and barrel to the Department of Women and Child Development. This latter Department, despite being designated the ‘nodal’ nutrition agency in the Government, had been functioning without the benefit and support of any in-house technical expertise in nutrition. Guidance which the Central Technical Committee of ICDS (under Dr B. N. Tandon), is eminently qualified to provide, is apparently not being effectively availed of. The shifting of the Food and Nutrition Board to the Department of Women and Child Development may help to partly improve its ‘technical’ competence and to enhance its credibility as a nodal nutrition agency to some extent.

But this will not happen if the scientists in the Board continue to be cramped and subordinated. It will be in the interest of the Department and of its image — as a nodal agency — to let the Board function as a semi-autonomous technical unit, without undue bureaucratic shackles, and to take full advantage of the inputs of the Central Technical Committee, which should be further strengthened and supported.

The Food Ministry also needs a competent nutrition cell. The shift of the Food and Nutrition Board away from the Food Ministry must have deprived it of whatever technical help it was receiving with respect to nutrition. There is a crying need for a proper nutrition orientation of our agricultural and food production programmes, which at present are hardly being effectively informed and guided by nutritional considerations. The shift of the Food and Nutrition Board to the Women and Child Development Ministry could turn out to be a case of ‘robbing Peter to pay Paul’ if immediate efforts to counter the consequential technical (nutrition) vacuum in the Food Ministry are not undertaken. The cause of nutritional betterment will not be served by musical chair exercises!

The Health Ministry currently oversees some major nutrition intervention programmes. There is an urgent need for a well staffed competent nutrition cell within the Ministry. Unfortunately the office of the Nutrition Advisor within the Ministry has been progressively downgraded and presently commands little clout and credibility. This is possibly a spin-off effect of the prolonged unedifying war of attrition between the technocracy and bureaucracy within the Health Ministry which has ultimately led not only to the weakening of its technical wing but also to the erosion of its own overall credibility and image.

A National Nutrition Policy, approved by the Cabinet, is coming up before the Parliament. The Government of India has also officially endorsed the ‘Declaration’ and ‘Plan of Action’ adopted at the recent International Conference on Nutrition. All these moves will turn out to be empty ritualistic exercises if effective (technical) instruments for the practical implementation of policies and programmes implicit in these declarations are not created. At present these hardly exist.

There are excellent centres and scientific resources within the country which can provide valuable technical support for the implementation of nutrition policies. It will be wise to make full use of such resources.

It is hoped that the announcement of the National Nutrition Policy will soon be followed by the enunciation of a concrete plan of action which will reflect national needs and interests.

We are grateful to UNICEF for a matching grant towards the cost of this publication.

Prof R. A. McCance

The passing away of Prof McCance marks the end of a glorious chapter in the history of nutrition science. The science of nutrition had been enriched, and hundreds of nutrition scientists around the world had been benefited and inspired by Prof McCance’s work which extended over a great part of this century. The McCance-Widdowson partnership has been a rewarding legend in the history of nutrition research.

Prof McCance belonged to the vanishing tribe of academics of the classical mould — austere, stern, simple, spartan and absolutely dedicated to the pursuit of science. He will rank among the all-time Greats in nutrition science.

It was a privilege for me to have known Prof McCance well and to have remained in correspondence with him over the years. Without in any way detracting from his greatness, it may be said that McCance owed his success, not a little, to his illustrious and gracious partner and colleague Dr Elsie Widdowson, who added lustre to his brilliance and perhaps also helped to smoothen occasional edges to his popular image. Students of nutrition around the world ardently hope that Dr Elsie Widdowson will continue to guide and inspire them in the years to come.

C. Gopalan