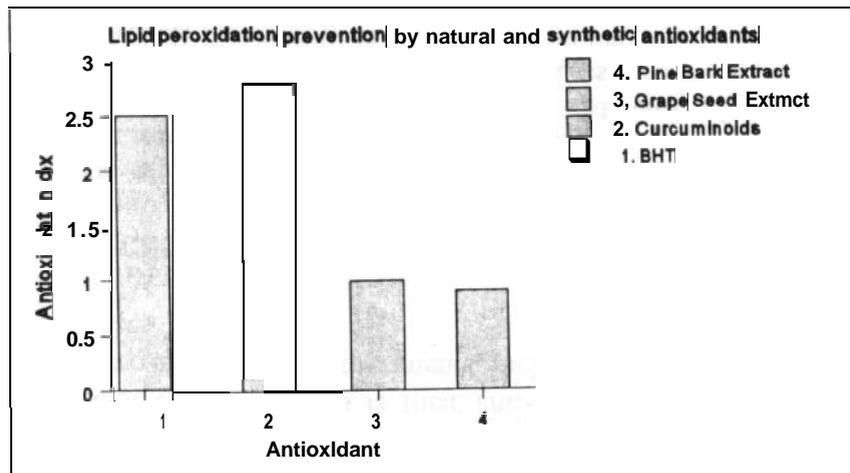


### 3. Overview of laboratory and clinical studies

The properties of curcuminoids in preventing build-up of tissue-injuring free radicals, particularly those responsible for the cardiovascular disease lipid peroxides, are among better known antioxidant properties of these compounds. Curcuminoids were shown to prevent lipid peroxides formation in a significantly higher degree than the pine bark extract, grape seed extract or a synthetic antioxidant like BHT, in an *in vitro* study.” The results of these experiments are indicated in the graph. The effectiveness of curcuminoids as antioxidants is evident.



(Ref. 17)

The particular blend of curcuminoids (2) used in the above experiment is known as C3 -Complex which has been shown to be more effective as an antioxidant than each of the components curcumin, demethoxycurcumin or bisdemethoxy curcumin used alone.” The effect of curcumin supplementation on serum lipid peroxides was studied in 10 healthy volunteers, to evaluate the antioxidant property of curcumin in preventing serum lipid peroxidation.<sup>18</sup> Administration of curcumin resulted in a

statistically significant reduction of serum cholesterol. These results clearly illustrate the potential role of curcuminoids in the prevention and treatment of cardiovascular disease.

Importantly, curcuminoids have been found both safe and effective antioxidants. Efficient antioxidants, like curcuminoids, scavenge free radicals at the cost of becoming weak free radicals themselves. These “second hand” free radicals are unreactive products, and do not pose a health hazard. Also the curcuminoid free radicals, unlike those of synthetic phenolics, e.g., BHT or BHA, are short-lived - a feature that further adds to their safety.

The other major biological property of turmeric and curcuminoids is their anti-inflammatory activity, comparable in strength to steroidal drugs and non-steroidal drugs like indomethacin and phenylbutazone.<sup>20,14,21,22</sup> Curcuminoids inhibit enzymes which participate in the synthesis of inflammatory substances in the body derived from arachidonic acid. For example, curcuminoids prevent the synthesis of several inflammatory prostaglandins and prostacyclines.<sup>23,24,25</sup> The overall anti-inflammatory action of curcuminoids is also related to their well-known antioxidant properties. For example, curcumin has been shown to inhibit lipid peroxidation, a phenomenon associated with antioxidant as well as anti-inflammatory activities.<sup>26,27</sup> The anti-inflammatory properties of curcumin were tested in a double-blind clinical trial in patients with rheumatoid arthritis.<sup>22</sup> Curcumin produced a significant improvement in all patients, and the therapeutic effects were comparable to those obtained with phenylbutazone.<sup>22</sup>

The nutritional role of turmeric extract and curcuminoids and anticarcinogens (preventing the development of cancer) and antimutagens (preventing damage to genetic material) has been the subject of recent research.<sup>28,29,30,31</sup> Both the turmeric extract and curcuminoids have been shown to inhibit carcinogenesis and mutagenesis in laboratory animals.

Curcumin was tested in patients with oral cancer.<sup>32</sup> Some patients responded with dramatic clinical improvement within days, while others responded gradually to the treatment. Administered to a group of chronic smokers, curcumin significantly reduced the urinary

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excretion of tobacco mutagens, and also enhanced the enzymatic efficacy to detoxify cigarette smoke mutagens and carcinogens.<sup>30,31</sup>

Curcuminoids have also been shown to exhibit anti-microbial properties. Extracts from turmeric as well as the active principles, the curcuminoids, were found to inhibit the growth of numerous gram positive and gram negative bacteria, fungi and the intestinal parasite, *Entamoeba histolytica*. Curcumin also inhibits *in vitro* production of aflatoxins - toxins produced by the mold *Aspergillus parasiticus*, which may grow and contaminate the poorly preserved foods.<sup>41</sup>

**Aflatoxin** is a potent biological agent causing injury to the liver, **often** resulting in liver cancer. Probably one of the most discussed properties of curcuminoids is their anti-HIV effect demonstrated during *in vitro* and *in vivo* experiments, including a limited number of human studies.<sup>15,16</sup>

### 4. Protection of the integrity of biological systems

In view of the recently discovered applications, the properties of curcuminoids can best be summarized as protective properties. This protective quality of turmeric exploited in its traditional role as a food preservative, translated into the results of current research which prove that turmeric protects the integrity of biomolecules in the body. Interestingly, preventing deterioration of food and preventing deterioration of tissue integrated nutrients, appear to be closely related to each other. The property of turmeric that prevents rancidity of meat, for example, helps to provide edible meat containing less oxidized fat or free radicals. On ingestion, this meat supplies nutrients, rather than damaging nutrient-radicals.

It seems likely that the same quality of turmeric that preserves the freshness of food that we eat, may also exert its role in the body by protecting living tissue from being exposed to degenerative processes. Clinical and laboratory research indicate that diets supplemented with turmeric or curcuminoids stabilize, and protect biomolecules in the body at the molecular level.<sup>34,35</sup> This stabilizing effect can be illustrated by the antioxidant, **anti-**mutagenic and anti-carcinogenic action of curcuminoids, both under *in vitro* and *in vivo* conditions.<sup>33</sup>

Turmeric and its active principles, the curcuminoids, can exert protection either directly, by shielding the biomolecule, or indirectly, by stimulating the

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natural detoxification and defense mechanisms of the body. For example feeding curcuminoids to experimental animals resulted in increased levels of the enzyme glutathione S-transferase, an important index of the efficiency of detoxification.<sup>35, 36, 37, 38, 39</sup> The detoxification processes help to preserve the integrity of biological systems.

Besides presenting the nutritional value of food and protecting the body from damaging free radicals, curcuminoids could arise during treatment with chemotherapeutic agents.<sup>40</sup> Turmeric extract and curcuminoids were tested for the prevention of tissue damage by some anticancer drugs and environmental toxins and pollutants. Anticancer drugs were generally more effective and less toxic when used in combination with turmeric or curcuminoids. Similarly, animals exposed to an environmental toxin like aflatoxin benefited from diets enriched with turmeric extract or curcuminoids.<sup>41</sup> Toxic effects produced by aflatoxin were significantly diminished by the curcuminoids supplementation.

Interestingly, curcuminoids also play a role in protecting some drugs from physio-chemical degradation. For example, addition of curcumin to the cardiovascular drug nifedipine, prevented degradation of nifedipine due to the ultra-violet light.<sup>42</sup> This protective effect increased with increasing concentrations of curcumin in nifedipine preparations.

It is thus evident that curcuminoids deserve special attention as compounds which protect biological systems internally and externally from the deterioration associated with aging and disease or drug related injury.

In the following chapters, the properties of curcuminoids which render them invaluable as a phytonutrient and therapeutic agent, will be reviewed.