

smokers and asbestos workers, augmented rather than reduced the occurrence of lung cancer (ATBC Study Group 1994). Later, it was recognized that  $\beta$ -carotene was administered alone in the intervention studies at 20–30 mg doses, much higher than the optimal daily intake in the epidemiological studies (about 4 mg), in which the diets comprised of other carotenoids and food constituents act synergistically with  $\beta$ -carotene (CARIG 1996). With these considerations, carotenoids regained their eminence, however the current emphasis is on carotenoids other than  $\beta$ -carotene.

*Lycopene.* Lycopene's possible role in the deterrence of cancer has enticed considerable attention (Gerster 1997; Clinton 1998; Sies and Stahl 1998; Rao and Agarwal 1999; Giovannucci 1999; Rissanen et al. 2002), with special emphasis on prostate cancer (Hadley et al. 2002; Giovannucci et al. 2002; Wertz et al. 2004; Stacewicz-Sapuntzakis and Bowen 2005). This carotenoid has also been associated with the prevention of CVD (Kohlmeier and Hastings 1995). A case-control study of 1379 men from 10 European countries (EURAMIC Study) revealed that a higher lycopene concentration in body fat was correlated with a lower risk of heart attack (Kohlmeier et al. 1997a).

*Lutein and Zeaxanthin.* Lutein and Zeaxanthin contribute to the yellow pigment in the macula of the human retina (Bone et al. 1988; Handelman et al. 1988) and also have been reported to be associated with the reduced risk for macular degeneration (EDCC 1993; Seddon et al. 1994), the primary cause of irrevocable blindness in the elderly. These two carotenoids have also been consistently associated with lowering the risk of cataracts (Moeller et al. 2000).

Although numerous studies support the protective outcome of carotenoids against chronic diseases, there have been some inconsistencies in the results, requiring more well-designed studies to be performed. The consumption of carotenoid-rich foods is widely recommended, but caution and more investigations are also advised to evaluate the benefits and risks of supplementation (Mayne 1996; Granado et al. 2003; Krinsky and Johnson 2005).

*Limonoids.* Limonoids are terpenes present in citrus fruit. Limonoids appear to provide chemotherapeutic activity by impeding the phase I enzymes and inducing phase II detoxification enzymes in the liver. D-Limonene, the most common monocyclic monoterpene, is found within orange peel oil, which inhibits pancreatic carcinogenesis induced in hamsters by N-nitrosobis(2-oxopropyl)amine and gastric carcinogenesis induced in Wistar rats by N-methyl-N'-nitro-N-nitrosoguanidine. Limonoids may also provide protection to lung tissue (Nakaizumi et al. 1997; Uedo et al. 1999).

### 2.2.2 PHENOLIC COMPOUNDS/POLYPHENOLS

Phenolic compounds are the most abundant and widely-distributed groups of substances in the plant kingdom, with more than 8000 phenolic structures presently known (Bravo 1998). These are secondary plant metabolites which act as the most abundant antioxidants in the human diet. These compounds are designed with an aromatic ring, carrying one or more hydroxyl moieties. According to the number of phenol rings and the structural elements that bind to these rings, they can be classified under several classes. Traditionally, they were categorized under two major groups of polyphenols, termed flavonoids and nonflavonoids.