Free Rad. Res. Comms., Vol. 17, No. 5, pp. 349–350
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LETTER TO THE EDITOR

DIETARY MANAGEMENT OF SICKLE CELL ANAEMIA WITH VANILLIN

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(*Received March 24, 1992; accepted March 25, 1992*)

Sir,

A recent report by Abraham *et al.*[1] suggests a management of sickle cell anaemia by dietary administration of vanillin, a flavouring agent added to a wide variety of foods.

Many additives are added to foods to protect the lipids present against the free radical chain reaction of lipid peroxidation. However, several such additives can potentially exert adverse effects against other biological components of the food matrix.[2–8]

Vanillin illustrates such dual properties. Whilst acting as an antioxidant in lipid assay systems,[2,3] vanillin was able to accelerate iron-dependent free radical damage to the carbohydrate deoxyribose.[2] Carnosol and carnosic acid (active components of rosemary extract) protected deoxyribose against free radical damage but stimulated DNA damage by bleomycin. Damage to DNA in the presence of a bleomycin-iron complex is one other method for assessing the potential pro-oxidant action of food additives and nutrient components.[2,4,6] Propyl gallate, a well known food antioxidant additive accelerates damage both to deoxyribose and to DNA.[2,8]

Other phenolic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are routinely used to inhibit lipid peroxidation and to extend the shelf life of foods. Phenolic antioxidant compounds are not devoid of adverse reactions at high concentrations in biological systems.[7] There is a growing interest in the ability of food additives following consumption, to inhibit (antioxidant) or to enhance (pro-oxidant) free radical reaction *in vivo*.[4]

Abraham *et al.*[1] confirmed and extended previous studies[9,10] on the anti-sickling activity of vanillin. A therapeutic dose of 1.0 to 4 gm/day or less was proposed. The use of the upper range of vanillin concentrations has to be viewed with caution. Repka and Hebbel[11] have also suggested caution on the administration of supraphysiologic doses of ascorbate to sickle cell patients. One approach in support of the suggestion by Abraham *et al.* may involve formulating diets containing in addition, a secondary antioxidant. The mechanism of pro-oxidant action is complex but free radicals are increasingly associated with a growing number of human diseases.[12]

References

1. D.J. Abraham, A.S. Mehanna, F.C. Wireko, J. Whitney, R.P. Thomas and E.P. Orringer (1991) Vanillin, a potential agent for the treatment of sickle cell anaemia. *Blood*, **77**, 1334–1341.
2. O.I. Aruoma, P.J. Evans, H. Kaur, L. Sutcliffe and B. Halliwell (1990) An evaluation of the antioxidant properties of food additives and of trolox c, vitamin E and probucol. *Free Radical Research Communications*, **10**, 143–157.
3. J. Burri, M. Graf, J. Lambelet and J. Loliger (1989) Vanillin: More than a flavouring agent a potent antioxidant. *Journal of the Science of Food and Agriculture*, **110**, 153–158.
4. O.I. Aruoma and B. Halliwell (1991) *Free Radicals and Food Additives*. London: Taylor & Francis.
5. M.J. Laughton, P.J. Evans, M.A. Maroney, J.R.S. Hoult and B. Halliwell (1991) Inhibition of mammalian 5-lipoxygenase and cycloxygenase by flavonoids and dietary additives. *Biochemical Pharmacology*, **42**, 1673–1681.
6. O.I. Aruoma, B. Halliwell, R. Aeschbach and J. Loliger (1992) Antioxidant and pro-oxidant properties of active rosemary constituents: Carnosol and carnosic acid. *Xenobiotica*, **22**, 257–268.
7. R. Kahl (1991) Protective and adverse biological actions of phenolic antioxidants. In H. Sies (ed.), *Oxidative Stress: Oxidants and Antioxidants*. London: Academic Press, pp. 245–273
8. J.M.C. Gutteridge and F. Xaio-Chang (1981) Enhancement of bleomycin-iron free radical damage to DNA by antioxidants and their inhibition of lipid peroxidation. *FEBS Letters*, **123**, 71–74.
9. R.H. Zaugg, J.A. Walder and I.M. Klotz (1977) Schiffs base adducts of hemoglobin. Modification that inhibit erythrocyte sickling. *Journal of Biological Chemistry*, **252**, 8542–8548.
10. C.R. Beddell, G. Kneen and R.D. White (1979) The antisickling activity of a series of aromatic aldehydes. *British Journal of Pharmacology*, **66**, 70P.
11. T. Repka and R.T. Hebbel (1991) Hydroxyl radical formation by sickle erythrocyte membranes: Role of pathogenic iron deposits and cytoplasmic reducing agents. *Blood*, **78**, 2753–2758.
12. B. Halliwell and J.M.C. Gutteridge (1989) *Free Radicals in Biology and Medicine*, 2nd edn. Oxford: Clarendon Press.

Accepted by Dr J.M.C. Gutteridge