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Vicine and Convicine: the Favic and Egg Weight Depressing Factors in Faba beans *(Vicia faba* L.) - A Review

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Faba beans *(Vicia faba* L.) are one of the most important pulse crops in the world, being consumed in large quantities in the Middle East, Far East and North Africa, particularly Egypt. Except for the presence of vicine and convicine and relatively low concentrations of several other antimetabolites, faba beans are an excellent source of protein with amino acid balance complimenting that of cereals (Marquardt, 1983; and Sarwar *et al* 1975).

Vicine and convicine were first isolated by Rithausen (1881), in *Vicia sativa*. These compounds were subsequently found in other species of *vicia* including *Vicia faba* (Manager *et al* 1969). The pyrimidine nucleoside structure of vicine as 2,6-diamino-4 , 5-dihyroxy pyrimidine, 5-(β-D-glucopyranose) and convicine as 2,4, 5-trihydroxy,6-aminopyrimidine,5-(β-D glucopyranose) was established by Bendich and Clement (1953).

In search of the favic causative agent in faba beans, Manger *et al* (1969) was aided by the fact that the agent had a capacity for oxidising glutathione (GSH) in glucose - 6 - phosphate dehydrogenase (G-6-PD) deficient red blood cells and some were sparingly soluble in water and exhibited in neutral solution a loss of GSH oxidising activity (Lin, 1963; and Manger *et al* 1969). The properties of the active fractions appeared similar to some pyrimidine derivatives known to occur in faba beans in the form of aglycones of β-glycosides termed vicine and convicine, the former being present in greater amounts than the latter (Manger *et al* 1969; Higazi and Read, 1974). The aglycones, divicine and isouramil can be obtained from the respective glycosides vicine and convicine by mild acid hydrolysis or by enzymatic splitting with β-glycosidase (Manger *et al* 1969).

The aglycones are highly unstable in the presence of oxygen and are almost instantaneously destroyed by boiling. The rate of their breakdown is most rapid at alkaline pH and falls with decreasing pH values (Manger *et al* (1969). At room temperature the half-life is in the order of 30 to 40 minutes. The breakdown of the pyrimidine aglycones is accelerated by traces of copper (Cu^{++}) and other heavy metals (Manger *et al* 1969).

All the characteristic properties of the aglycones are abolished by substitution of the hydroxyl group at C-5, such as that represented by the glycosidic linkage present in vicine and convicine (Manger *et al* 1969). These glycosides show none of the reducing properties of their aglycones, are heat stable and their ultraviolet spectra are different from those of their aglycones (Manger *et al* 1969).

Incubation of human red blood cells with the aglycones, divicine and isouramil resulted in a rapid fall in their glutathione (GSH) level. Addition of glucose prevented the injurious action on normal erythrocytes but not glucose 6-phosphate dehydrogenase (G-6-P D) deficient ones

(Manger *et al* 1969). The powerful capacity for oxidizing GSH exhibited by the pyrimidine aglycones *in vitro* is consistent with a possible causative role of these substances in precipitating the favic crisis (Lin and Ling, 1962; and Manger *et al* 1969). The conditions present for enzymatic release of aglycones from the glycosides, as well as the particular instability of these aglycones might account for the puzzling irregularity which characterizes the occurrence of favism in susceptible individuals, irrespective of the degree and frequency of their exposure to the noxious agent (Manger *et al* 1969). The term *favism* was coined in 1814 by the Italian physician L. Montano to designate an acute haemolytic anaemia following ingestion of broad beans (faba beans) or inhalation of pollen of the *Vicia faba* plant (Sansone *et al* 1958; and Manger *et al* 1969).

Faba beans contain a factor that depresses egg size in laying hens (Davidson, 1973; Robblee *et al* 1977; Campbell *et al* 1980 and Olaboro *et al* 1981a). This factor is present in faba bean protein concentrate in a concentrated form, is thermostable, is soluble in aqueous solutions, can be obtained as a white crystalline material and has been identified as being vicine (Olaboro *et al* 1981b; and Olaboro *et al* 1981c). Convicine when incorporated into the laying diet also induces egg size depression (13%) to approximately the same degree as that obtained with 1% vicine. Vicine when added to the laying diet at a concentration of 1% in addition to depressing egg size, also depressed egg production rate, total egg mass, yolk weight, yolk mass, packed cell volume, the fertility and hatchability of eggs and ratio of yolk height/diameter (Muduuli *et al* 1981; and Muduuli *et al* 1982). This latter parameter is an indirect measure of the fragility of the membrane.

In contrast, vicine increased the percentage of blood spots in the yolk, the plasma lipid concentration, plasma lipid peroxide concentration, degree of spontaneous hemolysis of erythrocytes and the weight of the liver (Muduuli *et al* 1981). The addition of vitamin E to the vicine containing laying diets, did not have a significant effect on most of the above parameters except that it dramatically improved the fertility and hatchability of eggs (Muduuli *et al* 1982).

The results with the laying hen give insight to what happens in favism in humans. The susceptibility of erythrocytes to hemolysis, the increased incidence of blood in the yolk, and decreased haematocrit concentration are similar to the haemolytic effects observed following the ingestion of faba beans by G-6-PD-deficient humans. The marked elevated plasma lipids and lipid peroxides together with the depressed amount of yolk which is primarily lipid in composition indicate that these compounds interfere with transport of fat across the yolk membrane.

The above observations together with the protective effects of vitamin E with regard to hatchability and fertility of eggs are consistent with the proposal, that the aglycones of vicine and convicine produce free radicals which not only react with erythrocytes but also other membranes and tissues to cause tissue damage and loss of functional properties.

The relative insensitivity of the young chick to vicine and convicine in contrast to the laying hen (Muduuli, 1982), may be attributed to their ability to re-synthesize reduced glutathione from NADPH in the presence of aglycones of vicine and convicine at a sufficiently rapid rate so as to neutralize their toxic effects (Chevion *et al* 1982). In the laying hen, there is a high demand for NADPH due to the high rate of fat synthesis (Griminger, 1976), which presumably results in limited availability of NADPH for other biological functions. In the presence of compounds such as vicine and convicine which induce oxidant stress, NADPH becomes limiting and as a result the laying hen is not able to neutralize these effects through the glutathione peroxidase system.

A similar, but more specific condition, occurs in human RBC. The net effect in both species is an increased sensitivity of the erythrocytes to the effects of vicine and convicine. Other tissues and organs, however are also affected in the laying hen which may be attributed to a general shortage of NADPH under stressful conditions as compared to the specific limitations of NADPH in the erythrocytes of G-6-PD deficient human.

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