I-23

Influence of ascorbate on the antiviral activity of quercetin derivatives.

R. VRIJSEN, L. EVERAERT and A. BOEYE, Dept. of Microbiology and Hygiene, Vrije Universiteit Brussel, Laarbeeklaan 103, B-1090 Brussels, Belgium

Several 3-methoxy derivatives of quercetin are known to exhibit antiviral activity against picornaviruses. To study the influence of the substitutions at ring position 3, we compared the antipoliovirus activity of 3-methylquercetin (3-MQ), luteolin and quercetin which at this position have a methoxy, a hydrogen or a hydroxy group, respectively 50% plaque reduction was achieved with 10 µM 3-MQ or 40 µM luteolin. No reduction in plaque number was observed with quercetin even at 100 µM.

Quercetin is known to undergo oxidative degradation in aqueous solution. As expected for an oxidative process, the degradation was prevented by ascorbate. Therefore the antiviral effect of quercetin was reinvestigated using quercetin-ascorbate mixtures. In the presence of 100 µM ascorbate, 30 µM quercetin caused 50% plaque reduction. D- and L-ascorbate were equally active, whereas dehydroascorbate was not. Ascorbate by itself caused no plaque reduction. On the other hand, the antiviral effect of 3-MQ and luteolin, which do not undergo oxidative degradation, was only slightly enhanced by ascorbate. The findings suggest that vitamin c may preserve the antiviral effect of labile flavonoids, which are abundant in the human diet.

I-24

ANTIVIRAL ACTIVITY OF NATURAL 3-METHOXYFLAVONES

Lucia Van Hoof, Viviane Robbrecht, Dirk Vanden Berghe, N.De Meyer, Achiel Haemers and Arnold J.Vlietinck
Faculty of Medicine, University of Antwerp (UIA), B-2610 Antwerp, Belgium.

3-Methoxyflavones are characterized by a very specific and strong antiviral activity against picornaviruses such as polio, coxsackie and rhinoviruses. We isolated such compounds from Dodonaea viscosa (L.) Jacq., Vernonia amygdalina Del. and several Euphorbia spp. We also tested isolates from different citrus fruits, Pachypodanthium sp., Ricinocarpus muricatus Muell. Arg., Prunus avium var. Juliana and Gnaphalium graveolens. The antiviral activity of the 3-methoxyflavones was studied by means of the endpoint titration technique (EPTT) in liquid medium using VERO-cells.
SAR studies revealed the 3-methoxyfunction to be essential for antiviral activity, whereas hydroxyfunctions at the 5 and 4'positions diminished significantly not only the acute cytotoxicity, studied in the EPTT but also the chronic cytotoxicity, determined by cultivation of VERO and RPE-cells in the presence of the 3-methoxyflavones. Polysubstitution of the A-ring of 3-methoxy-5,4'-dihydroxyflavone with methoxyfunctions giving a 5,6,7,8 substitution pattern of the A-ring markedly decreased cytotoxic activity without affecting much antiviral potency, which resulted in more selective antiviral 3-methoxyflavones.