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INTRINSIC ACTIVITY

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*MEETING ABSTRACT*

## A2.6

### The influence of antacids on the permeability of gliclazide – PAMPA model of the gastrointestinal mucosa

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**Background:** Gliclazide is a sulfonylurea derivative that is used for the treatment of diabetes melitus type 2. Since it causes gastrointestinal side effects such as gastroesophageal reflux, patients often use it along with antacids. In case of a failure of antidiabetic therapy, drug–drug interactions should always be suspected but patients generally do not inform physicians about the concomitant use of antacids. The aim of the study was to examine the effect of antacids on the permeability of gliclazide *in vitro* and to gain a better insight into the mechanisms responsible for the observed effects.
**Methods:** The permeability of gliclazide alone and in the presence of antacids (sodium bicarbonate, calcium carbonate, aluminium hydroxide, hydrotalcite and calcium carbonate / magnesium carbonate) was investigated using the parallel artificial membrane permeability assay (PAMPA), in a set of four media (three buffers pH 1.2, pH 4.5, pH 6.8 and in water). After a six-hour incubation period, the concentrations of gliclazide were measured by the HPLC method, and permeability coefficients were determined. The pH values of all groups were tested in order to determine how much the antacids changed the pH of the medium.
**Results:** At pH 1.2, groups with calcium carbonate, hydrotalcite and the combination calcium carbonate / magnesium carbonate showed significantly better permeability of gliclazide than the control group. At pH 4.5, calcium carbonate and the combination calcium carbonate / magnesium carbonate significantly increased the permeability of gliclazide, while sodium bicarbonate and aluminium hydroxide reduced permeability. All groups with antacids at pH 6.8 showed reduced permeability of gliclazide in comparison to the control group.
**Discussion:** Considering the results, it can be concluded that antacids significantly decrease, but also increase the permeability of gliclazide at different pH values, which may consequently affect the bioavailability of gliclazide. The tested pH values of all groups suggested that the permeability of gliclazide is largely influenced by the degree of its ionization which depends on the change in pH of the environment by antacids. Nevertheless, also other mechanisms may be involved such as complex and salt formation.
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**Keywords:** drug absorption – drug interactions – gliclazide – antacids – parallel artificial membrane permeability assay (PAMPA)

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