Cyclodextrins in Various Drug Formulations

8.0. Formulations, Applications, Forms and Administration Routes

Drugs are practically never administered as pure substances. They are formulated as liquid, semisolid, or solid formulations.

Although the intrinsic pharmacological effect of the drug substances is responsible for the drug's ultimate pharmacological effects, the intensity and the duration of the therapeutic effects can be influenced very much by the composition of the formulation. Excipients or bases can determine the safety and effectiveness of the therapy.

Beyond the stabilizing effects, CDs reduce the reactivity of drugs in the solid state, enhance their dissolution rate and solubility, reduce the bad taste in the mouth and can convert sticky lipids, liquids or even gaseous substances to crystalline solids, which can easily be mixed and tabletted.

The justification, the benefit and possible disadvantages of an addition of CDs or CD derivatives are essentially determined by the formulation and the administration route.

Regarding the formulations of CDs, one can differentiate between the administration of:

- solid inclusion compounds;
- mixtures of CD and drug;
- solutions of drug and CD.

Most interesting is the use of solid inclusion compounds, which can be formulated especially as solid formulations for oral use or for parenteral use after solution in a suitable solvent.

SOLID FORMULATIONS

In the case of solid formulations containing drug–CD complexes, or mixtures of drug and CD, problems can arise during the formulation process, or during storage...
of the finished product. Addition of water during the manufacturing process, for instance, can result in undesirable reactions. A solid inclusion compound can dissociate into its constituents in the presence of water. CDs which are dissolved in water – even in small amounts – can exert catalytic effects. The use of water or of aqueous granulation fluids should be avoided in such cases. A dry granulation process or direct compression has to be preferred (see Section 7.5).

The stability of solid formulations which contain a solid inclusion compound is generally guaranteed if humidity is excluded. Interactions of an inclusion compound with other constituents of the formulations are scarcely to be expected.

Excipients which could be candidates for inclusion should be excluded.

SEMISOLID FORMULATIONS

It is difficult to make a safe prediction of the behaviour of CDs and their inclusion compounds in semisolid formulations. Interactions with the usual suppository bases must be taken into consideration. Components of cocoa butter, adeps solidus, or polyethylene glycols, which are frequently used bases, may be included in the CD cavity. These bases are mixtures of substances of similar structure. Reactions between ‘empty’ CD molecules and these constituents are possible during the melting process associated with the preparation, during storage, or after administration.

LIQUID FORMULATIONS

CDs and CD derivatives with good solubility enable the formulation of solutions of poorly soluble drugs. Dissolved CDs can, however, in a few cases exert enzyme-like catalytic effects on the drug or other constituents of the formulation. Interactions between CD and constituents of the formulation can also result in an undesirable incompatibility. Such interaction can, for example, decrease the effect of a preservative. In most cases, however, the use of CDs – particularly of CD derivatives – is advantageous in liquid formulations.

8.1. Peroral and Oral Solid Preparations (Dosage Forms): Powders, Granules, Capsules, Tablets

Peroral formulations are primarily provided for absorption from the gastrointestinal tract while oral formulations are intended to be absorbed from the oral cavity. This