

Design and Synthesis of Polymers for Enhanced Solubility

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Abstract

Purpose: Many drugs fail to reach the consumer market due to various reasons. One possibility that a drug can fail to reach the later stage of clinical trials in the developmental process is poor solubility (often due to formulation and pharmacokinetic issues). Often, these are the rate limiting steps in a drug's bioavailability. Thus, less soluble drugs are likely to be poorly absorbed and, therefore, have a lesser effect on the body. This study aims to design and develop a polymer that can be combined with various drugs and act to increase the drug's solubility and bioavailability.

Methods: Radical polymerization methods were used in the synthesis of the modified PVPs with different chain lengths. These modified PVPs were characterized using NMR, LCMS, and GPC techniques. A series of poorly soluble drugs were used to assess the solubility enhancement capability of the polymers at two different concentrations (1% and 5% solutions). The primary outcome was a calculated Solubility Ratio (SR) comparing AUC of drug/water solution to drug/polymer solution obtained from HPLC.

Results: Improved SRs did occur with some of the modified PVPs. Drugs that showed some improved water solubility include: estrone, griseofulvin, clotrimazole, amiodarone, carbamazepine, phenytoin, and sulfadiazine.

Conclusions: The developed polymers improved the water solubility of a few of the drugs used in this study. The improvements in solubility appear to rely on the concentration, length, and cap of the designed polymers. Further research is needed to determine relationships between the PVP size, the modifier and the physicochemical properties and structure of poorly soluble drugs. These findings, however, are promising in that a newly created polymer solution could be added to formulations of poorly soluble drugs to increase their bioavailability. This means that currently approved drugs could be given at lower strengths or less frequently when combined with the polymer. Additionally, drugs that may have failed approval due to poor water solubility could have another opportunity at the developmental process if combined with the polymers.