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Effect of PH on the solubility of practically insoluble sorafenib by comparing polyamidoamine (PAMAM) dendrimers with β-cyclodextrin

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Background and Aims: This study is the first report of the solubilization of sorafenib (SFB) , a water insoluble drug, by polyamidoamine (PAMAM) dendrimers and β-cyclodextrin (β-CD).
Methods: For this study whole generations (G4 and G5) and a half generation (G4.5) of PAMAM dendrimers have been used. The aqueous solubility of sorafenib was measured in the presence of dendrimers and β-cyclodextin at 30 ◦ C at pH 4, 7.4, and 10 using the solvent evaporation method. The amount of solubilized SFB was measured by HPLC-UV method. FTIR and UV-Vis spectroscopy were used to confirm complexation.
Results: The solubility of sorafenib ranged from 0.96 to 2.9 mcg/ml between pH 4-10. The full generations (G4.0 and G5.0) of PAMAM dendrimer showed maximum solubilizing effect at pH4, and for G4 it was higher than G5 about 2 folds. The half generation (G4.5) dendrimer increased the solubility of SFB most at pH 7.4. In the presence of aqueous solutions of β-CD at the pH 7.4 and 10 a slightly increase in aqueous solubility of sorafenib was observed. But aqueous solutions of β-CD did not increase the aqueous solubility of SFB at pH 4. The highest increase in sorafenib was observed with G4.0 PAMAM dendrimer at pH 4 (36 folds).
Conclusions: This study is the first report of the solubilization of sorafenib by β-CD complexation or the interaction between the drug and PAMAM dendrimers. From the phase solubility studies, it was found that whole generation PAMAM dendrimers increased SFB solubility most in pH 4 followed by pH 10 and G4.5 most increased SFB solubility at pH 7.4. The maximum solubilizing effect was for G4 PAMAM dendrimers at pH 4 up to 36 folds. β-CD did not or slightly increased the solubility of SFB.

Keywords: Sorafenib; Solubilization; PAMAM dendrimers; Beta-cyclodextrin