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# A NOVEL HYBRID-NANOCOMPOSITE OF ALPHA-GLUCOSYL STEVIA AND SURFACTANT: FOR DISSOLUTION AND ABSORPTION ENHANCEMENT OF INSOLUBLE DRUGS

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## ABSTRACT

We have already reported the micelle-like nanostructure formation by the association of α-glucosyl stevia (Stevia-G) in aqueous media. The present study demonstrated the nanocomposite formation based on a mixed-micelle formation with Stevia-G and sodium dodecyl sulfate (SDS). The usage of nanocomposite of Stevia-G/SDS for the improvement of the dissolution and absorption of pranlukast hemihydrate (PLH) was evaluated. The simple mixing of tricomponent of SDS, Stevia-G and PLH extremely increased the amount of dissolved PLH compared to that of the untreated PLH, bicomponent of PLH/Stevia-G (1/10 w/w) and PLH/SDS (1/0.5 w/w). The concentration of dissolved PLH was enhanced with increased of amount of added surfactant. The concentration of dissolved PLH from tricomponent of PLH/Stevia-G/SDS (1/10/0.5 w/w/w) was 20-fold compared to that of the untreated PLH. To investigate the dissolution enhancement effect of Stevia-G/SDS mixture, the pyrene $I_1/I_3$ ratio was plotted versus Stevia-G concentration. The pyrene $I_1/I_3$ ratio of SDS/Stevia-G mixture indicated a sigmoidal curve at the lower Stevia-G concentration compared to the Stevia-G solution. The critical micelle concentration of Stevia-G, SDS and mixture of SDS/Stevia-G solution calculated from the pyrene $I_1/I_3$ plot was about 16, 2.5 and 0.8 mg/mL, respectively. This result indicates that the mixed-solution of Stevia-G/SDS provides the hydrophobic core around pyrene molecules in lower stevia-G concentration, leading to the mixed micelle-like properties based on the nanocomposite formation between Stevia-G and SDS.

The nanocomposite of Stevia-G and SDS showed no cytotoxicity to Caco-2 cells at mixture of 0.1 % SDS and 1 % Stevia-G solution, whereas 0.1 % SDS solution showed the high toxicity to Caco-2 cell. As shown in the in vivo study of PLH after oral administration in rats (Fig.1), the areas under the curve (AUC) up to 8 h for untreated PLH, the bicomponent of PLH/Stevia-G (1/2 w/w), and tricomponent of PLH/Stevia-G/SDS (1/2/0.5 w/w/w) were 138.7±42.6, 231.9±49.6, and 438.8±63.8 ng·h/mL, respectively. AUC of the tricomponent of PLH/Stevia-G/SDS (1/2/0.5 w/w/w) was 3.1-fold that of the untreated PLH.

These results suggest that the nanocomposite formation of Stevia-G/SDS is a very easy and useful way to enhance the dissolution and absorption profile of poorly-water soluble drug without special treatment.