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## Development of 4-Allylpyrocatechol Loaded Self-Nanoemulsifying Drug Delivery System for Enhancing Water Solubility and Antibacterial Activity against Oral Pathogenic Bacteria

Authors: Pimpak Phumat, Sakornrat Khongkhunthian, Thomas Rades, Anette Müllertz, Siriporn Okonogi

Abstract: Self-nanoemulsifying drug delivery systems (SNEDDS) containing 4-allylpyrocatechol (AP) extracted from Piper betle were developed to enhance water solubility of AP by using modeling and design (MODDE) program. The amount of AP in each SNEDDS formulation was determined by using high-performance liquid chromatography. The formulation consisted of 20% Miglyol®812N, 40 % Kolliphor®RH40, 30 % Maisine®35-1 and 10 % ethanol was found to be the best SNEDDS that provided the highest loading capacity of AP. (141.48 $\pm$ 15.64 mg/g SNEDDS). The system also showed miscibility with water. The particle shape and size of the AP-SNEDDS after dispersing in water was investigated by using a transmission electron microscope and photon correlation spectrophotometer, respectively. The results showed that they were a spherical shape, having a particle size of 34.27  $\pm$  1.14 nm with a narrow size distribution of 0.17  $\pm$  0.04. The particles showed negative zeta potential with a value of -21.66  $\pm$  2.09 mV. Antibacterial activity of AP-SNEDDS containing 1.5 mg/mL of AP was investigated against Streptococcus intermedius. The effect of this system on S. intermedius cells was observed by a scanning electron microscope (SEM). The results from SEM revealed that the bacterial cells were obviously destroyed. Killing kinetic study of AP-SNEDDS was carried out. It was found that the killing rate of AP-SNEDDS against S. intermedius was dose-dependent and the bacterial reduction was 79.86  $\pm$  0.45 % within 30 min. In comparison with chlorhexidine (CHX), AP-SNEDDS showed similar antibacterial effects against S. intermedius. It is concluded that SNEDDS is a potential system for enhancing water solubility of AP. The antibacterial study reveals that AP-SNEDDS can be a promising system to treat bacterial infection caused by S. intermedius.

Keywords: SNEDDS, 4-allylpyrocathecol, solubility, antibacterial activity, Streptococcus intermedius

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