University of Macau

Abstract

PREFORMULATION AND ORAL ABSORPTION MECHANISTIC STUDIES ON ZEDOARY TURMERIC OIL

by Leng Wei

Thesis Supervisor: Dr. Ying ZHENG
Prof. Yitao WANG

Chinese Medicinal Sciences

Zedoary Turmeric, which is the rhizomes of three species of *Curcuma* including *Curcuma phaeocaulis*, *Curcuma kwangsiensis* and *Curcuma wenyujin*, has been used over a long periods as a traditional Chinese medicine for removing blood stasis and alleviating pain. The essential oil extracted from the herb medicine which consisted most of the bioactive components in Zedoary Turmeric is also named Zedoary Turmeric Oil (Ezhu oil). It has many biological activities, such as anti-tumor, anti-inflammatory and anti-virus activities. Up to now, the researches concerning oral absorption and metabolism mechanism of Zedoary Turmeric Oil are less, the problems of which components could be well absorbed and could use as the marker compound for analysis purpose need to be solved.

The Caco-2 cell line is derived from a human colorectal carcinoma. The utility of this cell line stems from the fact that the Caco-2 cells differentiate spontaneously to enterocytes under conventional cell culture conditions upon reaching confluence on porous polycarbonate membranes, and thus resemble small intestinal epithelium. Several active transport systems that are located in the intestinal epithelium (such as sugars, amino acids, dipeptides, bile acids and cobalamin intrinsic factor) are also expressed in Caco-2 cells. This model has well in vitro-in vivo correlations for drug absorption. The research about oral absorption mechanism of Zedoary Turmeric Oil using Caco-2 cell model has not been seen in publications. The current study will use Caco-2 cell model to investigate the absorption mechanism of Zedoary Turmeric Oil and the influence of transport directions, drug concentrations and other compositions to the permeability of active compounds in the essential oil.

Caco-2 cell model was applied to investigate the transport mechanism of Zedoary Turmeric Oil and some of its active components, including curdione, germacrone, furanodiene and curcumol. Apparent permeability coefficients of above active compounds and Zedoary Turmeric Oil across Caco-2 cell monolayers were measured as a function of direction of transport and concentration of each component. In addition, the effects of other components on the permeability of curdione and germacrone were also investigated.

The apparent permeability coefficients (P_{app}) of curdione, germacrone and curcumol are all at 10^{-5} cm/s level, which is comparable to transcellular marker of propranolol and did not significantly change with transport directions and drug concentrations ($P>0.05$). Furanodiene and other high lipophilic components in Zedoary Turmeric Oil (e.g. furanodiene, curzerene and β-elemene) could not transport across Caco-2 cell monolayer. Components other than selected compounds in Zedoary Turmeric Oil did not interfere with the permeability coefficient of curdione and germacrone ($P>0.05$). No metabolites could be detected in receiver side during the transport study with Zedoary Turmeric Oil and selected active compounds.

The above results indicated that the transcellular transports are predominantly by passive diffusion for Zedoary Turmeric Oil and its selected active components. The high lipophilic components in Zedoary Turmeric Oil, e.g. furanodiene, could not transport across the Caco-2 monolayer and most of them were uptake into cell monolayer and could not reach to receiver side. Other components in Zedoary Turmeric Oil did not influence the transport of the active components in the essential oil.

Keywords: Zedoary Turmeric Oil; Caco-2 cell absorption model; Absorption mechanism; Passive diffusion