(+)-Catechin 在家兔體內之藥物動力學研究

Pharmacokinetic study of (+)-Catechin in rabbits

中文摘要

(+)-Catechin(3,3',4',5,7-tetrahydroxyflavan)是屬於一種 flavonoid 之化合物,在植物界分佈廣泛,它具有顯著的肝保護作用.目前在歐洲臨床上口服治療急性濾過性病毒肝炎,及避免肝毒性物質和酒精所引起之肝傷害.本實驗除了對(+)-Catechin 之分析方法及血液內之安定性再探討外並選擇家兔爲實驗動物,以不同途徑之投與方式,包括靜脈投與,腹膜腔內(intraperitonael)投與以及口服投與,來觀察(+)-Catechin 在家兔體內之藥物動力學的表現, 進一步來探討(+)-Catechin 在家兔體內之生體可用率 (bioavaila- bility).本實驗所使用的分析方法採用固-液抽提(solid-liquid extraction)的方式,使用 aluminum oxide 爲抽提之物質,並用螢光檢測器(fluorescence detector),增加分析之靈敏度,最低檢測濃度可達 10ng/ml.選擇八隻家兔靜脈注射三種不同劑量，15、20、30mg/kg 之 (+)-Catechin,在此劑量範圍下呈 Dose Independent 之藥物動力學,其數據處理過程符合二室模式,經由靜脈注射 30mg/kg,腹膜腔內投與 30mg/kg 與口服 100mg/kg 之(+)-Catechin 於家兔體內的結果得知,其代謝屬於線性藥物動力學(linear pharmacokinetic),而其生體可用率分別爲 0.85 ±0.36 與 0.02±0.01,顯示(+)-Catechin 經由肝門脈吸收後,其肝臟首渡效應(first pass effct),即通過肝臟時只有 15%的藥量會被代謝掉;而口服投與較高劑量 100mg/kg 之(+)-Catechin,其生體可用率僅有 2% ,其原因可能是由於藥物在腸胃道時之吸收不佳或代謝太快所導致。

英文摘要

The naturally occurring flavanol,(+)-Catechin(3,3',4',5, 7-tetrahydroxyflavan),which is found widespread in plants has been used to traet acute viral hepatitis and prevent hepatic disorders induced by ethanol or hepatotoxic substance in Europe. Up to now, there were few reports about the phar- macokinetics of (+)-Catechin in human and animals reported. In present syudy, the pharmacokinetic of(+)-Catechin with different doses and administrative routes in rabbits was studied. In analytical study, aluminum oxide was used as solid phase extraction material in solid-liquid extraction process. After extraction, a reverse phase HPLC method with fluorescence detector was developed. Under this chromatogra- phic condition,

good linearity of standard curve (range 20~ 8000ng/ml, $r=0.9999$) of (+)-Catechin was obtained and the detective limitation of (+)-Catechin was 10ng/ml. After three different doses of (+)-Catechin (15,20,30mg/kg), there were no significant differnces between elimination rate constant and dose of I.V. administrated. The AUC (area under curve) obtained from I.V. administration of (+)-Catechin was propor- tional to various doses. This means a dose independant phar- macokinetics of (+)-Catechin in rabbits ($Y=1.1299X+3.9029$, $r=0.9585$ $p<0.001$). The intraperitoneal(30mg/kg) and oral (100mg/kg) administration of (+)-Catechin also showed a linear pharmacokinetics. The bioavailability of intraperitoneal and oral administration were 0.85 ± 0.36 and 0.02 ± 0.01, respectively. This means about 15% of (+)-Catechin may be metabolized by liver(hepatic first pass effect), and the bioavailability of oral administration may result from poor absorption of (+)-Catechin in the gastro-intestinal tract.