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The effects of wine-processing on ascending and descending: The distribution of flavonoids in rat tissues after oral administration of crude and wine-processed *Radix scutellariae*

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Baicalin (Pubchem CID: 64982)
Wogonoside (Pubchem CID: 29927693)
Baicalein (Pubchem CID: 5281605)
Wogonin (Pubchem CID: 5281703)
Oroxylin A (Pubchem CID: 5320315)
Chrysin (Pubchem CID: 5281607)
Scutellarin (Pubchem CID: 185617)
Oroxylin A-7-O-glucuronide (Pubchem CID: 44567248)
Scutellarein (Pubchem CID: 5281697)
Apigenin (Pubchem CID: 5280443)

ABSTRACT

Ethnopharmacological relevance: Ascending and descending theory is a core principle of traditional Chinese medicine (TCM) theories. It plays an essential role in TCM clinical applications. Some TCM medicine has specific properties, which could alter the inclination and direction of their actions. The properties of the ascending and floating process of one herbal medicine are affected by means of herb processing. Wine-processing, which is sautéing with rice wine, is one of the most popular technologies of herb processing. Wine-processing increases the inclination and direction of its actions, thereby producing or strengthening their efficacy in cleaning the upper-energizer heat.

Radix scutellariae, the dried roots of *Scutellaria baicalensis* Georgi, is a well-known TCM used for the treatment of inflammation, pyrexia, jaundice, etc. Recently, wine-processed *Radix scutellariae* was normally applied in clinical studies for the treatment of upper-energizer syndrome. In order to investigate the effects of wine-processing on ascending and descending of *Radix scutellariae*, the comparative study of distribution of flavonoids in rat tissues of triple energizers (SanJiao-upper, middle, lower jiao) after oral administration of crude and wine-processed *Radix scutellariae* aqueous extracts was carried out.

Materials and methods: The rats were randomly assigned to two groups and orally administered with crude and wine-processed *Radix scutellariae* aqueous extracts, respectively. At different pre-determined time points after administration, the concentrations of compounds in rat tissue homogenate were determined, and the main tissue pharmacokinetic parameters were investigated. Tissue pharmacokinetic parameters including AUC_{0-t}, $t_{1/2}$, T_{max} and C_{max} were calculated using DAS 2.0. An unpaired Student *t*-test was used to compare the differences in tissue pharmacokinetic parameters between the two groups. All the results were expressed as arithmetic mean ± S.D.

Results: The parameters of C_{max} and AUC_{0-t} of some flavonoids in wine-processed *Radix scutellariae* were remarkably increased ($p<0.05$, $p<0.01$, $p<0.001$) in the rat upper-energizer tissues (lung and heart) compared with those of the crude group. However, in the rat middle- and lower-energizer tissues (spleen, liver and kidney), the C_{max} and AUC_{0-t} of some flavonoids were significantly decreased ($p<0.05$, $p<0.01$) compared with the crude group. The main explanation for these differences seems to the effects of wine-processing on ascending and descending theory.

Conclusions: All of these differences in the distribution of triple energizers after oral administration of crude and wine-processed *Radix scutellariae* aqueous extracts may lead to the increase of efficacy on the upper-energizer tissues and were in compliance with the ascending and descending theory. Therefore, wine-processing was recommended when *Radix scutellariae* was used for cleaning the upper-energizer heat and humidity. The obtained knowledge can be used to evaluate the impact of

Abbreviations: TCM, Traditional Chinese Medicine; LLOQ, lower limits of quantification; QC, quality control; DP, declustering potential; CE, collision energy; CXP, collision exit potential; RE, relative error; FDA, Food and Drug Administration; $t_{1/2}$, the half-time; C_{max}, maximum plasma concentration; T_{max}, time to reach the maximum concentrations; AUC_{0-t}, area under concentration–time curve

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these differences on the efficacy of both the drugs in clinical applications and might be helpful in explaining the effects of wine-processing on ascending and descending theory.

1. Introduction

The benefits of Traditional Chinese Medicine (TCM) seem to be related to the content of active compounds in TCM for medicinal purposes. Tissue distribution is a vital approach to investigate the major target sites and interpret the disposition of compounds in vivo. Considering the growing concern of a potential beneficial role of compounds in human health, detailed disposition studies of compounds in vivo in TCM for medicinal purposes need to be carried out.

The herb-processing method, which is based on the dialectical treatments of medical needs in TCM and the drugs' characteristics, has been assisting TCM in developing reasonable pharmaceuticals of Chinese medicine. There are various traditional ways of processing herbs, such as frying with sand or oil, sautéing with rice wine or wheat bran, steaming with water or rice wine, braising with rice wine or licorice liquids, etc. (Jin and Wang, 2004). These processes contribute to increasing potency, reducing toxicity and altering the original effects. The main mechanisms underlying herb processing were mainly attributed to the changes in the composition of active compounds in the herbs (Cai and Gong, 2009). Moreover, changes in chemical characteristics subsequently induced changes in absorption and distribution of TCM in vivo.

The ascending and descending theory (the complete term is ascending and descending, floating and sinking theory) is a core principle of TCM theories. In TCM theories, the ascending and floating theory indicates whether the action of a particular drug is going upward or outward within the body, while the descending and sinking theory implies going downward and inward. These activities will counteract the pathologic actions going in the opposite directions.

Based on the ascending and descending theory, TCM has some special affiliates for certain organs of the body associated with particular diseases. The ascending and descending theory is the concept with both qualitative and positioning analyses of TCM. The foundation of ascending and descending theory has the selective effect of active compounds appearing in triple energizers

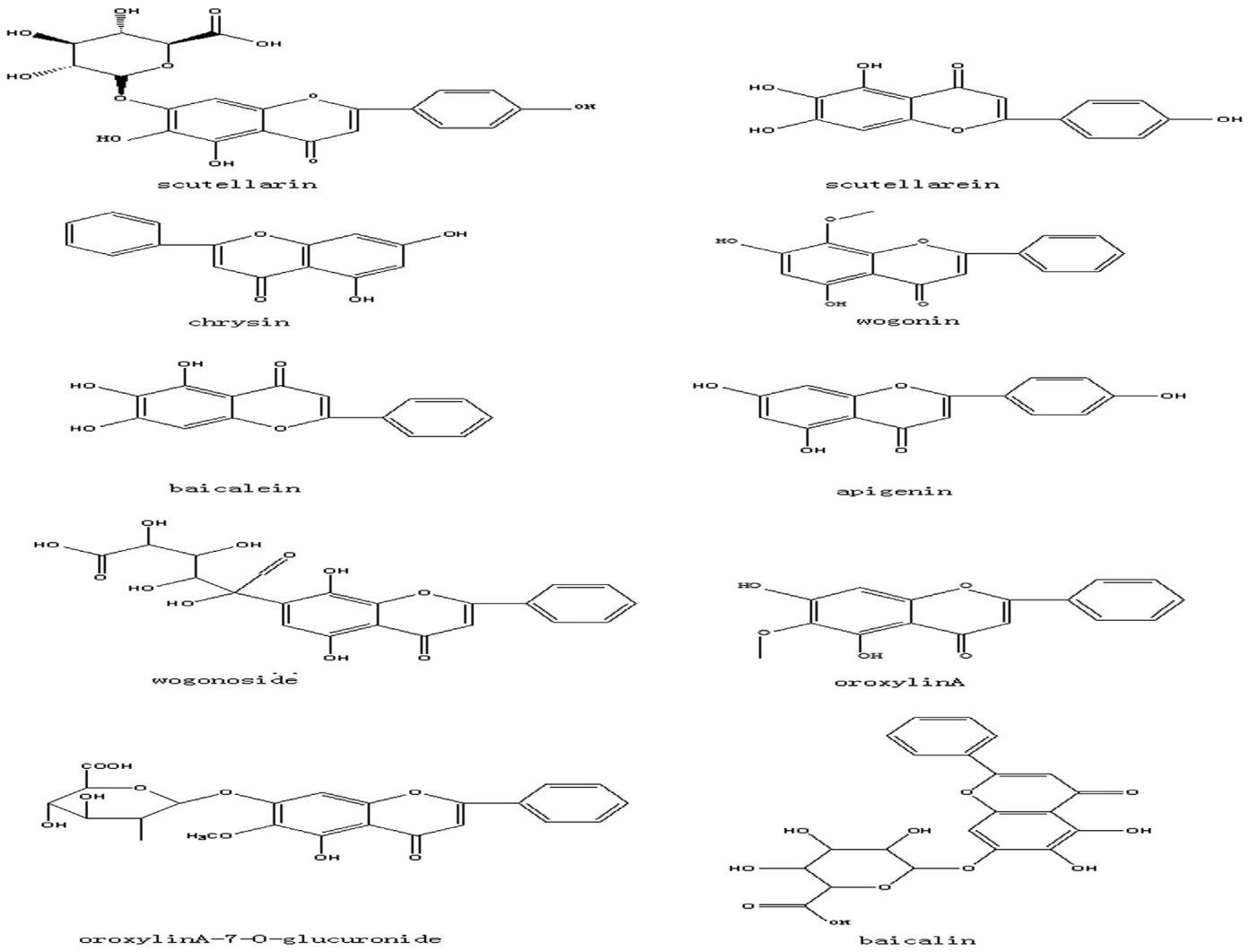

Fig. 1. Chemical structures of ten flavonoids: scutellarin, scutellarein, chrysin, wogonin, baicalein, apigenin, wogonoside, oroxylin A-7-O-glucuronide, oroxylin A, baicalin.