“901”复方感冒冲剂的药剂学研究

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摘要 介绍了“901”复方感冒冲剂的工艺、质量控制及稳定性。制得的冲剂符合中国药典（1990版）的要求；对其主药黄芩、柴胡进行了薄层定性鉴别；以黄芩甙为指标，采用一阶导数光谱法进行了含量测定；加速实验预测有效期为1.97年。

关键词 “901”复方感冒冲剂 药剂学研究 黄芩甙 一阶导数光谱法

“901”复方感冒冲剂系根据民间验方以黄芩、柴胡、鸭趾草、黄芪、白花蛇舌草、甘草等6味中药为原料研制而成。药效实验表明对亚州流感药毒FM_1株有显著抑杀作用，并兼有良好的退热效果，目前正在进行临床验证。在这基础上，对其进行了制备、质控等一系列研究，以期为今后的生产提供一些有效的数据。

1 材料及仪器

1.1 中药材均购自南京市药材公司；所有液体化学试剂均为分析纯；黄芩甙标准品（中国药品生物制品检定所）；硅胶GF_{254}（青岛海洋化工厂）；聚酰胺-6薄膜（浙江黄岩化学实验厂）；CMC-Na（上海化学试剂采购供应站）。

1.2 直立式薄膜蒸发器；H66025T超声清洗机（无锡超声电子设备厂）；UV-1型三用紫外分析仪（上海顾村电光仪器厂）；岛津UV-300自记式分光光度计（日本）。

2 方法与结果

2.1 制备工艺：用正交设计法优选“901”复方感冒冲剂的制备工艺。简单流程如下：

中草药⟹煎煮⟹薄膜浓缩⟹醇沉⟹制粒⟹干燥灭菌⟹包装

通过比较打分，确定其最佳工艺条件为煎煮次数3（每次1h），薄膜浓缩温度90℃（真空度0.09MPa），稠膏比重1.3～1.4，浸膏-糖粉-糊精（1∶0.5∶1），颗粒干燥温度60℃。

2.2 冲剂质量常规检查：本冲剂外观呈黄色、颗粒状，大小色泽均一，颗粒度符合药典要求；采用铝塑包装，每袋12g。

烘干法测定该冲剂样品3批，含水量在3%～4%之间，达到药典标准。另测定3批样品，其平均重量差异小于±0.2%，小于药典标准±0.5%的要求。

溶化性能实验，3批样品均在5min内全部溶化。

2.3 薄层层析（定性鉴别）

2.3.1 黄芩的鉴别：取“901”复方感冒冲剂、阴性对照品各1g，加70%乙醇10ml，超声波提取5min，过滤后备用；另取黄芩甙标准品少许，加70%乙醇1ml溶解，备用。

分别取滤液和标准品液各5μl，点于同一聚酰胺-6薄膜，用36%醋酸展开，UV-1型紫外分析仪365nm下观察棕色斑点（图1）。

2.3.2 柴胡的鉴别：取冲剂样品、阴性对照品（不含柴胡）、柴胡标准药材（本校标本馆）各1g，加乙醚10ml，超声波提取10min，放置12h，过滤，滤液挥去乙醚加甲醇0.5ml溶解，备用。

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分取上述3试液各0.5μl，点于硅胶GF$_{254}$-CMC-Na板上，展开剂为氯仿-苯-甲醇(1∶5∶1)，展开后置紫外分析仪254nm下观察，结果见图1。

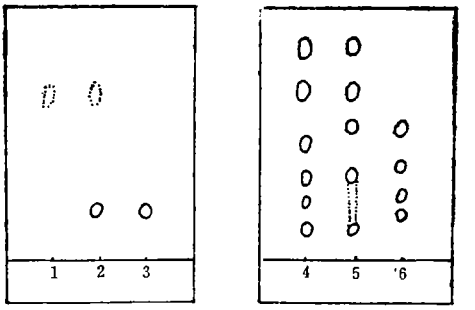

图1 黄芩、柴胡层析图

1-阴性对照 2-冲剂样品 3-黄芩甙标准品
4-柴胡标准药材 5-冲剂样品 6-阴性对照

2.4 定量分析："901"复方感冒冲剂成分复杂较难分离，故用一阶导数光谱法在不经分离的条件下测定其主要成分黄芩甙的含量。

2.4.1 紫外光谱扫描：称取样品粉末、阴性对照品粉末各100mg，黄芩甙标准品2mg，分别加入70%乙醇适量，超声波提取20min，过滤，滤液定容至200ml，备用。

取上述3溶液在200～400nm波长范围内扫描，其零阶导数光谱见图2。由图可见，样品与标准样品在276nm处均有最大吸收峰且吸收曲线基本平行，阴性对照品在该处虽有一定吸收度，曲线却较为平坦。这为导数光谱法测定黄芩甙含量提供了一个信息。

另取上述3溶液在200～400nm范围内以4nm为间隔进行一阶导数光谱扫描（图3）。可见，阴性对照品基本为一直线，干扰消除。由图中找出黄芩甙峰谷对应的中间波长分别为263nm和284nm，故测定波长先261与265nm，282与286nm。

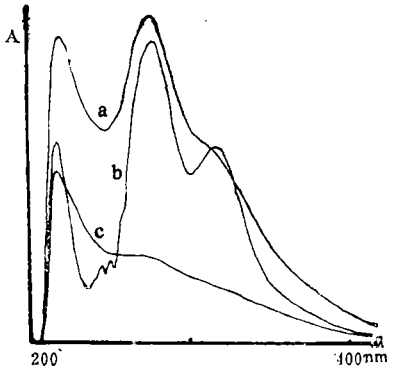

图2 零阶导数光谱图

a-样品 b-标准品 c-阴性对照

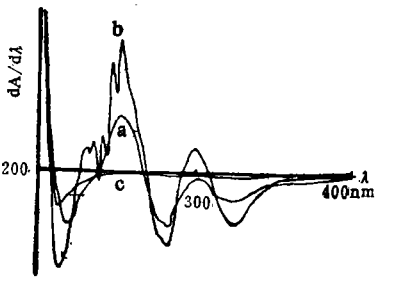

图3 一阶导数光谱图

a-样品 b-标准品 c-阴性对照

2.4.2 标准曲线绘制：精密称取干燥至恒重的黄芩甙标准品10mg，以70%乙醇溶解并定容于100ml容量瓶中。精密吸取0.5、1、2、4、8ml于50ml容量瓶中稀释至刻度，测定261与265nm，282与286nm处的吸收值，算出峰谷差值ΔA。以浓度C（μg/ml）为横坐标、ΔA为纵坐标绘制标准曲线，回归方程为$\Delta A = 0.0156C - 0.0085$，$r = 0.9999$。

2.4.3 加样回收试验：精密称取阴性对照品50mg，加入黄芩甙标准品1mg，以70%乙醇适量超声波提取20min，过滤，滤液定容至200ml，测定吸收度求算ΔA，回收率$\bar{X} \pm S = 102 \pm 2\%$，RSD = 1.96%。

2.4.4 样品含量测定：精密称取冲剂样品80mg，加70%乙醇超声提取后配成250ml溶液，测定选定波长处的吸收度，结果见表1。

表1 样品含量测定结果

批号	样品数（n）	黄芩甙含量（%）	变异系数（%）
920410	5	2.05±0.06	2.93
920421	4	2.03±0.05	2.46

2.5 加速稳定性试验：参照文献4，采用简易法，选取90、100℃2个温度进行恒温加速实验。根据恒定温度下lgC－t曲线求出$t_{0.9}^{90℃}$与$t_{0.9}^{100℃}$，然后由$\lg(t_{0.9}^{1}/t_{0.9}^{2}=E(T_2-T_1)/2.303RT_1T_2$求出活化能E，最后可知$t_{0.9}^{25℃}$。

精称70mg冲剂样品6份，置于90℃恒温箱中，分别于0、2、4、8、18、24h时取出测定黄芩甙含量，结果见表2。

表2 60°C恒温加速试验

时间 t（h）	0	2	4	8	18	24
样品（mg）	70.8	72.6	6.99	72.7	70.6	70.4
含量 C（%）	2.05	1.89	1.76	1.61	1.46	1.39
lgC	2.311	2.277	2.246	2.206	2.163	2.146

回归方程 $\lg C=-0.00654t-1.714$ $r=-0.9515$

同样，精称70mg样品6份，置于100℃恒温箱中，于0、1、2、4、9、12h时取出测定含量，结果见表3。

表3 100°C恒温加速试验

时间 t（h）	0	1	2	4	9	12
样品（mg）	70.9	67.9	66.6	71.4	68.4	72.1
含量C（%）	1.98	1.59	1.52	1.49	1.24	1.12
lg C	2.298	2.202	2.183	2.174	2.095	2.04

回归方程 $\lg C=-0.0171t-1.754$ $r=-0.9416$

由两lgC-t回归方程得$t_{0.9}^{90℃}=7.00h$，$t_{0.9}^{100℃}=2.68h$。故E＝25.83Kcal/mol，求得$t_{0.9}^{25℃}=1.97y$。因此可以预测“901”复方感冒冲剂室温下贮存2年有效。

3 小结

3.1 本实验在冲剂制备过程中采用薄膜浓缩、低温干燥，避免了药物有效成分长时间遇热破坏，提高了成品质量。

3.2 黄芩甙含量测定过程中，加入乙醇后应在6h内进行吸收度测定。时间过久，则黄芩甙成分有变化，吸收度有偏移。

3.3 进行稳定性试验时，样品从恒温箱取出后应立即冷却至室温，否则结果也会受影响。

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ABSTRACTS OF ORIGINAL ARTICLES

Studies on the Chemical Components of Chinese Drug Yuzhizi I. Hederagenin 3-O-Glycosides of the seeds of Austral Akebia (*Akebia trifoliata* var. *australis*)

Ma Shuangcheng, Chen Dechang and Zhao Shujie

Yuzhizi is the seed of *Akebia quinata* (Thunb.), *A. trifoliata* (Thunb.) Koidz. and *A. trifoliata* (Thunb.) Koidz. var. *australis* (Diels) Rehd.. Two triterpenoid saponins of hederagenin 3-O-glycosides have been isolated from the seeds of *A. trifoliata* (Thunb.) Koidz. var. *australis* (Diels) Rehd. for the first time. They were identified by spectroscopic (EI-MS, FAB-MS, ^{1}H, ^{13}CNMR and 2DNMR) and chemical methods (acid/base hydrolysis) as I: 3-O-β-D-xylo-pyranosyl-(1→2)-α-L-arabinopyranoside hederagenin (saponin B); II: hederagenin 3-O-β-D-glucopyranosyl-(1→2)-α-L-arabinopyranoside (saponin C).

(Original article on page 171)

Studils on the Liposoluble Components from the Rhizomes of Fortune's Drynaria (*Drynaria fortunei*)

Zhou Tongshui and Zhou Ronghan

Fifteen liposoluble compounds were isolated and identified from the rhizomes of *Drynaria fortunei* (Kunze) J. Sm.. They are: diploptene (I); hop-21-ene (II); diplopterol (III); fern-9(11)-ene (IV); cyclolaudenol (V); cyclomargenol (VI); cyclolaudenone (VII); n-dotriacontanic acid (VIII); β-sitosterol (IX); 25-en-cycloartenol (X); 25-en-cycloartenone (XI); 24-en-cycloartenol (XII); 24-en-cycloartenone (XIII); 5-stigmasten-3-ol (XIV); 5-stigmasten-3-one (XV). Apart from I, IV and IX, the rest had not been found in this fern since.

(Original article on page 175)

Studies on the Chemical Constituents of Leaves of Sweet potato (*Ipomoea batatas*) Introduced from Brazil

Xiang Rende, Ding Jianxin, Han Ying, et al

Seven compounds were isolated from the alcohol extract of leaves of *Ipomoea batatas* Lam, by column chromatography on silica gel. They were identified by physical and chemical methods as quercetin-3-glucoside (I), kaempferol-4′, 7-dimethyl ether (II), ombuin (III), quercetin (IV), quercetin-3′, 4′, 7-trimethyl ether (V), β-sitosterol (VI) and sucrose (VII). All of them were isolated from this plant for the first time.

(Original article on page 179)

Pharmaceutical Study on "901" Anti-Influenza Complex Granule

Tang Minghui, Shao Lizheng, Xie Yanjun, et al

The manufacturing process, quality Control and Stability test of "901" anti-influenza complex granule were presented. The granule tallied with requirements of Chinese Pharmacopoeia (1990th edition). It s main components (*Scutellaria baicallensis* Georgi. and *Bupleurum chinese* DC.) were identified with TLC. First derivative spectrometry was used to determine

the content of baicalin in this preparation. As a result of stability test, the shelf life at 25°C is estimated to be 1.97 years.

(Original article on page 182)

Studies on Effective Compositions of Pinecone Ⅱ. Determination of Polysaccharides in Cone of Chinese Pine (*Pinus tabulaeformis*)

Li Haozhi, Lu Yongjun, Bai Gang, et al

Quantitative determination of polysaccharides in pine cones by phenol-sulfuric acid method was studied, and the effects of concentration of phenol-sulfuric acid and reaction temperature on color formation were investigated. It was found that the absorbance is linearly correlated to polysaccharide concentrations between 10~78μg/ml (r=0.9999). The analytical recovery was 99.8%, CV% was 1.2% and the minimal detectable concentration was 5μg/ml.

(Original article on page 185)

Artificial Neural Network Method for Quality Estimation of Traditional Chinese Medicine

Cai Yudong, Gong Jiawen, Cheng Zhaonian, et al

An artificial neural network method for quality estimation of traditional Chinese medicine was suggested, and quality of Hou-Po was estimated by the proposed method in comparison with the analytical results of gas-liquid chromatography. The successful rate reached 100%. The results showed that the neural network method is reliable, and therefore may be referred to as an effective technique for the quality estimation of traditional Chinese medicine.

(Original article on page 187)

Protective Effect of Paeonol Against Ischemia Reperfusion Damage in Cardiac Mitochondria Membrane of Rats

Zhang Weiguo and Zhang Zhishan

60mg/kg·d ip, of paeonol were given to rats for 15 days. The myocardial ischemia reperfusion injury model was produced by occluding the left coronary artery and releasing the occlusion in rats. This significantly decreased myocardial Ca^{++}-ATPase activities and CH/PL radical, FFA content, improved mitochondrial membrane fluidity and kept them away from oxygen free radical damage. These results indicated that paeonol has membrane protective effect on myocardial ischemia reperfusion injury probably by inhibiting the oxygen free radicals and subsequent lipid peroxidation.

(Original article on page 193)

An Inquiry into Preparing Diarrhea Model of Mice and Application of Diarrhea Index

Zhou Gannan, Hu Zhihua, Wang Yaxian, et al

In Order to screen antidiarrhea drugs, the standard operation of mice diarrhea model replicated with leave of Cassia angustifolia vahl was introduced. In experiments, diarrhea index expressed with loose stool incidence rate multiplied by loose stool grade was used as main index. It thoroughly mirrors indi.