

## 二陈汤方加减对2型糖尿病并发脂肪肝模型大鼠血糖、血脂、胰岛素抵抗以及肝功能和肝脏脂肪变的影响\*<sup>\*</sup>

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### Effect of pingtang recipe on blood glucose, lipid, resistance of insulin, liver function and changes of hepatic lipid in rats with type 2 diabetes mellitus complicated with fatty liver

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### Abstract

**AIM:** To investigate effect of pingtang recipe characterized by resolving phlegm, removing damp by diuresis and promoting blood circulation by removing blood stasis, on blood glucose, lipid, resistance of insulin, liver function and pathomorphological changes of hepatic lipid in rats with type 2 diabetes mellitus (DM) complicated with fatty liver.

**METHODS:** The experiment was completed in the Animal Experimental Center in Medical College of Xiamen University from April to November of 2004. ① Totally 40 healthy Wistar rats aged 7 weeks old of half gender were selected in this study. Twelve rats were selected as normal control group and fed with ordinary diet (mass of main components: carbohydrate 0.6, protein 0.22, fat 0.1, others 0.08; soya bean oil especially in fat), and other rats were fed with high-calorie diet (mass of main components: carbohydrate 0.4, protein 0.13, fat 0.4, others 0.07; animal lipid especially in fat). After 2 months, rats in normal control group were injected with 0.1 mol/L pH4.2 citric-acid buffer solution and other 28 rats were injected with 25 mg/kg streptozotocin (STZ). Blood glucose was tested after 72 hours, if fasting blood glucose (FBG)  $\leq$  16.7 mmol/L, the rats were diagnosed as DM. So 24 rats successfully made into diabetic models. ② Totally 24 diabetic rats were divided randomly into model group and pingtang recipe group with 12 in each group. Rats in normal group were fed with ordinary diet, but other rats were fed with high-calorie diet. Rats in pingtang recipe group were perfused with 8 mL/(kg·d) pingtang recipe once a day which consisted of chenpi, banxia, fuling, jiangchan and dilong provided by dispensary of our hospital and made into concentration of 2 g/mL raw materials. Rats in normal control group and model group were perfused with the same volume of water for 16 weeks. ③ Enzyme-linked immunosorbent assay (ELISA) was used to assay levels of insulin, calculate hepatic index (hepatic wet weight/body mass  $\times$  100%) and sensitive index of insulin  $\ln [1/(\text{fasting blood glucose} \times \text{fasting insulin})]$ . Meanwhile, degeneration of hepatic fat and degrees of inflammatory necrosis were observed under light microscope. Scores of inflammatory

activity: Inflammatory activity of chronic hepatitis and inflammatory activity of fibrosis were contained average area (P), internal lobule (L), debris necrosis (PN) and bridging necrosis (BN). According to mild, moderate and severe degrees, each item was regarded as 1, 3 and 4 points as the following formula: P+L+2 (PN+BN). Contents of serum triacylglycerol (TG), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), glutamic oxalacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), albumin and total protein were assayed with relevant kit provided by Shanghai Jiuqiang Biotechnology Company Limited. Fasting blood glucose was measured with oxidase method 8 weeks before modeling and 16 weeks after modeling. ④ Measurement data, ranked data and rate difference were compared with average *t* test, rank sum test and statistical test respectively.

**RESULTS:** Four rats failed to be models, 24 rats entered the final analysis. ① Hepatic index in model and pingtang recipe group was higher than that in normal control group 16 weeks after modeling ( $P < 0.01$ ). ② Level of fasting blood glucose in model group and pingtang recipe group was higher 8 and 16 weeks after modeling than that before modeling and in normal control group ( $P < 0.01$ ), but that in pingtang recipe group was lower than that in model group 8 and 16 weeks after modeling ( $P < 0.05$ ). ③ Level of blood insulin in model group was higher than that in normal control group and pingtang recipe group 16 weeks after modeling ( $P < 0.01$ ). ④ Sensitive index of insulin in model group was lower than that in normal control group and pingtang recipe group 16 weeks after modeling ( $P < 0.01$ ). ⑤ Levels of serum TG and LDL-C were higher in model group and pingtang recipe group than those in normal control group 16 weeks after modeling ( $P < 0.01$ ), but those in pingtang recipe group were lower than those in model group ( $P < 0.05$ ). ⑥ Level of HDL-C in model group and pingtang recipe group was lower than that in normal control group 16 weeks after modeling ( $P < 0.05$ ), but that in pingtang recipe group was higher than that in model group ( $P < 0.05$ ). ⑦ Activities of GPT and GOT in model group and pingtang recipe group were higher than those in normal control group 16 weeks after modeling ( $P < 0.05-0.01$ ), but those in pingtang recipe group were lower than those in model group, and there was not significantly different ( $P > 0.05$ ). ⑧ Scores of inflammatory activity in liver: Those in model group and pingtang recipe group were higher than those in normal control group 16 weeks after modeling ( $P < 0.01$ ), but there was no significant difference between model group and pingtang recipe group. ⑨ Pathomorphological changes in liver: There was no abnormality in normal control group 16 weeks after modeling. Diffuse fatty degeneration was observed in hepatocyte of rats in model group and pingtang recipe group, but changes of hepatic lipid was not different between two groups. **CONCLUSION:** Pingtang recipe can improve blood glucose, lipid, resistance of insulin and liver function in rats with type 2 diabetes mellitus complicated with fatty liver, but cannot relieve the damage of hepatic histology.

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### 摘要

目的:观察具有化痰利湿、活血化瘀功效的二陈汤方加减干预2型糖尿病并发脂肪肝大鼠血糖、血脂、胰岛素的抵抗状况,以及脂肪肝模型病理形态学的变化。

方法:实验于2004-04/11在厦门大学医学院动物实验中心完成。①选用健康Wistar大鼠40只,7周龄,雌雄各半。随机抽取12只为正常对照组,喂以普通饲料(其中各成分质量分数如下:碳水化合物0.6、蛋白质

0.22 脂肪 0.1 其他 0.08 脂肪以豆油为主),其余则喂养高热量饲料(其中各成分质量分数如下:碳水化合物 0.4,蛋白质 0.13,脂肪 0.4,其他 0.07 脂肪以动物油脂为主)。2 个月后,正常对照组的大鼠一次性腹腔注射链脲佐菌素 25 mg/kg。72 h 后查血糖 $\geq 16.7$  mmol/L 为糖尿病大鼠,造模成功 24 只。②将 24 只糖尿病大鼠随机分为 2 组:模型组和二陈汤方加减组,每组 12 只。正常对照组喂以普通饲料,其余 2 组均喂养高热量饲料。二陈汤方加减组大鼠按 8 mL/(kg·d)剂量灌胃二陈汤方加减药物,由陈皮、半夏、茯苓、僵蚕及地龙等组成(上述中药由本院中药房提供),由本院药剂科制备成浓缩液(含生药 2 g/mL),1 次/d;正常对照组和模型组灌胃等量的自来水,均连续干预 16 周。③然后采用 ELISA 法测血胰岛素水平,计算肝指数(肝湿重/体质量 $\times 100\%$ )和胰岛素敏感指数  $\ln\{1/(\text{空腹血糖} \times \text{空腹胰岛素})\}$ ;光镜下评估肝脂肪变性和炎症坏死程度。炎症活动度计分[慢性肝炎炎症活动度及纤维化计分方案炎症活动度计分分为汇管区(P)、小叶内(L)、碎屑坏死(PN)及桥接坏死(BN)4 项,每项依病变轻、中、重程度分别计以 1、3、4 分,计分公式为 P+L+2(PN+BN)]。按照上海九强生物技术有限公司提供相应试剂盒说明书测定血清三酰甘油、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、谷草转氨酶、谷丙转氨酶、白蛋白及总蛋白水平。分别于造模前、造模后 8 周及造模后 16 周采用氧化酶法测定空腹血糖。④计量资料、等级资料、率差异比较分别采用两样本均数 *t* 检验、秩和检验、两样本率差别的统计意义检验。

结果:由于造模失败脱落 4 只,最终进入结果分析 36 只。①肝指数:造模后 16 周模型组和二陈汤方加减组明显高于正常对照组( $P < 0.01$ )。②空腹血糖水平:造模后 8 和 16 周模型组及二陈汤方加减组均明显高于造模前和正常对照组( $P < 0.01$ )。造模后 8 和 16 周二陈汤方加减组明显低于模型组( $P < 0.05$ )。③血胰岛素水平:造模后 16 周模型组明显高于正常对照组和二陈汤方加减组( $P < 0.01$ )。④胰岛素敏感指数:造模后 16 周模型组明显低于正常对照组和二陈汤方加减组( $P < 0.01$ )。⑤血清三酰甘油和低密度脂蛋白胆固醇水平:造模后 16 周,模型组和二陈汤方加减组明显高于正常对照组( $P < 0.01$ ),二陈汤方加减组明显低于模型组( $P < 0.05$ )。⑥血清高密度脂蛋白胆固醇水平:造模后 16 周,模型组和二陈汤方加减组明显低于正常对照组( $P < 0.05$ ),二陈汤方加减组明显高于模型组( $P < 0.05$ )。⑦血清谷丙转氨酶和谷草转氨酶活性:造模后 16 周,模型组和二陈汤方加减组明显高于正常对照组( $P < 0.05 \sim 0.01$ ),二陈汤方加减组低于模型组,但差异不明显( $P > 0.05$ )。⑧肝脏炎症活动度计分:造模后 16 周,模型组及二陈汤方加减组明显高于正常对照组( $P < 0.01$ ),但模型组与二陈汤方加减组差异不明显。⑨肝脏病理学形态变化:造模后 16 周,正常对照组大鼠肝脏无异常病变。模型组及二陈汤方加减组均出现弥漫性肝细胞脂肪变性,且两组肝脂肪变情况无区别。

结论:二陈汤方加减可在一定程度上能改善糖尿病并发脂肪肝大鼠的血糖、血脂水平,胰岛素抵抗状况及肝功能指标,但不能减轻肝脏组织学病变。

关键词:糖尿病,非胰岛素依赖型;脂肪肝/中药疗法;疾病模型;动物

## 0 引言

脂肪肝是遗传、环境、代谢等因素所致的以肝细胞脂肪变性为主的临床病理综合征,其发病机制尚未完全明确。2 型糖尿病常伴有肥胖、高脂血症,因此更容易发生脂肪肝。本实验旨在观察二陈汤方加减在降血糖、调节血脂紊乱、改善胰岛素抵抗方面的作用及对大鼠脂肪肝模型病理形态学的影响。

## 1 材料和方法

设计:完全随机分组设计,对照动物实验。

单位:厦门市中西医结合糖尿病研究所。

材料:实验于 2004-04/11 在厦门大学医学院动物实验中心完成。选用健康 Wistar 大鼠 40 只,7 周龄(雌雄各半,体质量 200~250 g,由厦门大学实验动物中心(许可证号 SYXK(闽)2004-0004)提供。动物饲

养环境:温度 20~26 °C,日温差 $< 4$  °C,相对湿度 40%~70%。

药物与试剂:二陈汤方加减(平糖方)由陈皮、半夏、茯苓、僵蚕及地龙等组成;上述中药购自本院中药房,由本院药剂科制备成浓缩液(含生药 2 g/mL)。链脲佐菌素购自美国 Sigma 公司,以 0.1 mL/L pH 4.5 柠檬酸缓冲液溶解,新鲜配制而成。血糖、血三酰甘油、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、谷丙转氨酶、谷草转氨酶、白蛋白及总蛋白测定试剂盒均购自上海九强生物技术有限公司;胰岛素测定试剂盒购自美国 DRG 公司。

主要仪器:全自动生化分析仪为日本 Hitachi 公司产品;721 型分光光度计为上海精密科学仪器有限公司产品。

设计、实施、评估者:实验设计为第一、二作者;干预实施与评估为全部作者,采用非盲法评估。所有评估者均接受正规科研培训。

方法:

模型建立:实验用大鼠饲养 1 周以适应环境,随机抽取 12 只为正常对照组,喂以普通饲料(其中碳水化合物 0.6,蛋白质 0.22,脂肪 0.1,其他 0.08,脂肪以豆油为主),其余则喂养高热量饲料(其中碳水化合物 0.4、蛋白质 0.13,脂肪 0.4,其他 0.07,脂肪以动物油脂为主)。2 个月后,正常对照组的大鼠一次性腹腔注射 0.1 mol/L pH 4.2 枸橼酸缓冲液,其余 28 只大鼠则一次性腹腔注射链脲佐菌素 25 mg/kg(链脲佐菌素溶于 0.1 mol/L pH 4.2 枸橼酸缓冲液中)。72 h 后查血糖 $\geq 16.7$  mmol/L 为糖尿病大鼠,造模成功 24 只。

分组及给药:实验用大鼠每日光照 12 h,自由饮水进食。将 24 只糖尿病大鼠随机分为模型组和二陈汤方加减组。正常对照组喂以普通饲料,其余 2 组均喂养高热量饲料。二陈汤方加减组灌胃以二陈汤方加减药物,按成人(60 kg)剂量的 10 倍[8 mL/(kg·d)]灌服,1 次/d;正常对照组和模型组灌胃以等量的自来水,均连续干预 16 周。

标本采取及观测:实验结束时处死各组动物。方法:隔夜禁食,次日以 20 g/L 戊巴妥钠溶液 1 mL/kg 腹腔注射麻醉后,迅速取出肝脏称湿重,并计算肝指数(肝湿重/体质量 $\times 100\%$ )。

测量体质量:分别于造模前及造模后 16 周,测量各组实验动物体质量。

测定空腹血糖及胰岛素:分别于造模前、造模后 8 周及造模后 16 周禁食 12 h 后,从心脏采血检测血糖,采用氧化酶法。于造模后 16 周采用 ELISA 法测血胰岛素水平,按照试剂盒说明书进行操作。

计算胰岛素敏感指数:参照李光伟等<sup>[1]</sup>的计算方法,胰岛素敏感指数= $\ln[1/(\text{空腹血糖} \times \text{空腹胰岛素})]$ 。

测定血脂及肝功能:造模后16周按照试剂盒说明书测定血清三酰甘油、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、谷草转氨酶、谷丙转氨酶、白蛋白及总蛋白水平。

病理学检查:造模后16周取肝左叶0.5 cm×1 cm×0.5 cm组织置于体积分数0.1甲醛溶液固定,常规苏木精-伊红染色。光镜下评估肝脂肪变性和炎症坏死程度。肝细胞脂肪变性程度判断按照脂变细胞占肝细胞的百分比<sup>[2]</sup>,炎症活动度计分[慢性肝炎炎症活动度及纤维化计分方案炎症活动度计分为汇管区(P)、小叶内(L)、碎屑坏死(PN)及桥接坏死(BN)4项,每项依病变轻、中、重程度分别计以1、3、4分,计分公式为P+L+2(PN+BN)]标准则参考1981年Knodell等<sup>[3]</sup>提出的慢性肝炎组织学活动指数,并结合王泰龄等<sup>[4]</sup>提出的慢性肝炎炎症活动度计分方案。

主要观察指标:二陈汤方加减对糖尿病大鼠肝指数、胰岛素敏感性指标、血脂、肝功能及肝脏病理形态学观察结果的影响。

统计学分析:数据由第五作者应用SPSS 10.0软件完成统计处理。计量结果均以 $\bar{x} \pm s$ 表示;计量资料、等级资料、率差异比较分别采用两样本均数 $t$ 检验、秩和检验、两样本率差别的统计意义检验。

## 2 结果

2.1 实验动物数量分析 纳入大鼠40只,由于造模失败脱失4只,最终进入结果分析36只。

### 2.2 统计推断

2.2.1 二陈汤方加减对糖尿病大鼠体质量及肝指数的影响 见表1。

表1 各组大鼠体质量及肝指数比较 ( $\bar{x} \pm s, n=12$ )

组别	体质量(g)		干预16周后肝指数(%)
	造模前	造模后16周	
正常对照组	237.50±15.42	318.50±39.74 <sup>a</sup>	3.12±0.84
模型组	240.42±15.68	412.25±23.58 <sup>bc</sup>	5.57±0.91 <sup>c</sup>
二陈汤方加减组	238.33±14.56	389.42±29.07 <sup>bcd</sup>	5.19±0.87 <sup>c</sup>

与造模前比较:<sup>a</sup> $P < 0.05$ ,<sup>b</sup> $P < 0.01$ ;与正常对照组比较:<sup>c</sup> $P < 0.01$ ;与模型组比较:<sup>d</sup> $P < 0.05$

2.2.2 二陈汤方加减对糖尿病大鼠空腹血糖和胰岛素及胰岛素敏感指数的影响 见表2。

表2 各组空腹血糖和胰岛素及胰岛素敏感指数比较 ( $\bar{x} \pm s, n=12$ )

组别	空腹血糖(mmol/L)			造模后16周胰岛素(mIU/L)	造模后16周胰岛素敏感指数
	造模前	造模后8周	造模后16周		
正常对照组	5.38±0.96	5.46±0.39	5.66±0.50	30.54±5.63	-5.12±0.35
模型组	5.40±0.37	20.52±1.70 <sup>ab</sup>	20.66±3.77 <sup>ab</sup>	47.49±6.57 <sup>b</sup>	-6.81±0.37 <sup>b</sup>
二陈汤方加减组	5.27±0.29	16.76±2.86 <sup>abc</sup>	14.43±3.17 <sup>abc</sup>	34.44±4.98 <sup>d</sup>	-6.19±0.32 <sup>d</sup>

与造模前比较:<sup>a</sup> $P < 0.01$ ;与正常对照组比较:<sup>b</sup> $P < 0.01$ ;与模型组比较:<sup>c</sup> $P < 0.05$ ,<sup>d</sup> $P < 0.01$

2.2.3 二陈汤方加减对糖尿病大鼠血脂的影响 见表3。

2.2.4 二陈汤方加减对糖尿病大鼠血清肝功能指标的影响 见表4。

表3 造模后16周各组大鼠血脂水平比较 ( $\bar{x} \pm s, n=12$ )

组别	三酰甘油(mmol/L)	低密度脂蛋白胆固醇(mmol/L)	高密度脂蛋白胆固醇(mmol/L)
正常对照组	5.66±0.50	0.72±0.24	1.64±0.16
模型组	20.66±3.77 <sup>b</sup>	4.87±0.86 <sup>b</sup>	1.01±0.15 <sup>a</sup>
二陈汤方加减组	11.43±1.17 <sup>bc</sup>	2.28±0.30 <sup>bc</sup>	1.36±0.17 <sup>ac</sup>

与正常对照组比较:<sup>a</sup> $P < 0.05$ ,<sup>b</sup> $P < 0.01$ ;与模型组比较:<sup>c</sup> $P < 0.05$

表4 造模后16周各组大鼠血清肝功能指标比较 ( $\bar{x} \pm s, n=12$ )

组别	谷丙转氨酶(nkat/L)	谷草转氨酶(nkat/L)	白蛋白(g/L)	白蛋白与球蛋白比值
正常对照组	695.14±155.03	1481.96±455.09	26.1±5.7	0.81±0.18
模型组	1491.97±338.40 <sup>a</sup>	3242.32±795.16 <sup>b</sup>	29.2±6.0	0.83±0.13
二陈汤方加减组	1243.58±331.73 <sup>a</sup>	2823.90±878.51 <sup>b</sup>	27.6±6.3	0.80±0.10

与正常对照组比较:<sup>a</sup> $P < 0.05$ ,<sup>b</sup> $P < 0.01$

2.2.5 二陈汤方加减对糖尿病大鼠肝脏脂变程度及炎症活动度的影响 造模后16周,正常对照组大鼠肝脏无异常病变。模型组及二陈汤方加减组均出现弥漫性肝细胞脂肪变性,几乎全部存在小叶内及汇管区炎症,有的存在汇管区变性及点状坏死,肝组织炎症细胞浸润以单核细胞、淋巴细胞为主,并有一些中性粒细胞浸润。脂变肝细胞以中央静脉周围最为明显,极度肿胀呈圆形,体积较正常明显增加,胞浆内充满大量脂肪空泡,界限不清,肝窦狭窄。模型组及二陈汤方加减组肝脂变情况无区别。肝脏炎症活动度计分:模型组及二陈汤方加减组明显高于正常对照组[(5.7±2.4)(5.8±2.1)(1.0±0.8)分, $P < 0.01$ ],但模型组与二陈汤方加减组差异不明显。

## 3 讨论

糖尿病患者常常伴有脂代谢紊乱,外周脂肪组织分解增加,游离脂肪酸形成增多,进入肝脏的脂肪酸增加,使肝脏内三酰甘油形成增多,因此更容易形成脂肪肝。胰岛素抵抗是2型糖尿病的重要致病机制。而胰岛素抵抗与脂肪肝之间有着密切的联系,越来越多的研究表明胰岛素抵抗可能是脂肪肝形成的启动因素<sup>[5,6]</sup>。外周胰岛素抵抗、游离脂肪酸增多,以及肝脏内三酰甘油的增加,促使了脂肪肝的形成,而反过来,脂肪肝加剧了高胰岛素血症及胰岛素抵抗,并诱导脂质过氧化、肝细胞炎症坏死及纤维化。

中医学一般将脂肪肝归于“胁痛”、“积聚”及“痰浊”等范畴。大多数学者认为脂肪肝的发生与饮食所伤和情志不遂有关,其病多实证,痰瘀互结是其基本病机。如杨继荪<sup>[7]</sup>认为本病的病因病机为饮食因素致气、血、痰、浊互相搏结,以痰瘀交阻为主。作者认为糖尿病合并脂肪肝的中医病机更为复杂,但痰瘀互结为其贯穿始终的主要病机和病理产物,故治疗上涤痰化瘀为其主要治则。二陈汤方加减药物由陈皮、半夏、茯苓、僵蚕、丹参及地龙等组成,具有化痰利湿、活血化瘀的功效。本实验以高热量饲料加小剂量链脲佐菌素建立的

接近于人类2型糖尿病的糖尿病大鼠并发脂肪肝为模型,观察二陈汤方加减在降血糖、调节血脂紊乱、改善胰岛素抵抗,以及对大鼠脂肪肝模型病理形态学的影响,结果表明:二陈汤方加减能降低体质量、调节血脂紊乱、改善胰岛素抵抗及降低肝指数和转氨酶,但对肝脏脂肪变性及炎症等无改善作用,提示具有涤痰化痰的二陈汤方加减虽在一定程度上有改善血脂紊乱、胰岛素抵抗以及转氨酶等作用,但不能减轻糖尿病大鼠的肝组织学病变。

本实验结果提示,导致糖尿病大鼠发生脂肪肝的原因可能不仅是脂代谢紊乱和胰岛素抵抗等,只有努力寻找导致糖尿病并发脂肪肝病理形态学损伤的原

因及中医病机,确立有针对性的治疗方法,才能提高中医药的疗效。

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·基础研究·

## 红花茯苓提取液防治四氯化碳性大鼠肝纤维化的作用\*★

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### Effect of honghua fuling extract liquid on hepatic fibrosis of rats induced by carbon tetrachloride

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#### Abstract

**AIM:** To study the character of hepatic damage induced by carbon tetrachloride and analyze the effect of compound honghua fuling extract liquid on its prevention and cure.

**METHODS:** The experiment was completed in the Experiment Animal Center, Pharmacological Laboratory and Central Laboratory of Guangdong Medical College from March 2003 to September 2005. Sixty SD rats of SPF grade were randomly divided into 6 groups: normal control group, model control group, positive control group, compound honghua fuling extract liquid 0.5 kg/L group, 1 kg/L group and 2 kg/L group with 10 of either gender in each group. Three dosages of compound honghua fuling extract liquid were provided by Technological Medicament Empolder Center of Guangdong Medical College. The compound was used honghua, fuling and gancaotopickup 3 times to get the dose of 2 kg/L, twice distilled water to dilute to get the dose of 0.5 kg/L and 1 kg/L. All the animals were given 600 g/L carbon tetrachloride arachis oil on the basis of 3 mL/kg subcutaneous injection once per 3 days for 7 weeks for the model of hepatic fibrosis except the control group. And the effects of compound honghua fuling extract liquid on histological change, serum hyaluronic acid, serum alanine aminotransferase, asparagic acid transaminase, total protein (TP), albumin (Alb) and weigh of viscera in hepatic tissue were observed in each dosage group. All the results were compared with colchicines to estimate the effect and character of

compound honghua fuling extract liquid on preventing and curing hepatic damage induced by carbon tetrachloride.

**RESULTS:** Totally 60 rats entered the final analysis. ① Changes of liver: Liver index in model group was increased 2.4 times than that in control group ( $P < 0.01$ ), and histopathological showed that most of hepatic cells in model group were degenerated seriously and fibrin tissue was proliferated clearly. But fiber proliferation was not observed in normal control group and hepatic fibrosis was reached 100% ( $P < 0.05$ ). There was not significantly different from that in crocus group. Hepatic indexes decreased 1.4, 1.7 and 2.3 times as compared with those in model group respectively ( $P < 0.05$ ). ② Changes of serum indexes: Content of hyaluronic acid in crocus group was decreased 3 times as compared with that in model group ( $P < 0.01$ ), 2.2, 2.3 and 2.6 times in compound honghua fuling extract liquid 0.5 kg/L, 1 kg/L and 2 kg/L groups respectively; activities of Alanine aminotransferase were decreased 1.6, 1.5 and 2 times as compared with those in model group respectively; activity of asparagic acid transaminase was obviously decreased ( $P < 0.05$ ); content of albumin was increased, especially that in 0.5 kg/L compound honghua fuling extract liquid group was 1 time than that in model group ( $P < 0.05$ ). ③ Change of portal vein pressure: The portal vein pressure in model group was higher than that in normal group, but there was no significant difference, and there were no significant differences among the six groups ( $P > 0.05$ ).

**CONCLUSION:** Compound honghua fuling extract liquid can prevent hepatic fibrosis after liver damage induced by carbon tetrachloride, decrease content of transaminase, and increase content of protein in rats.

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#### 摘要

**目的:** 观察四氯化碳诱导的大鼠肝损害的特点, 并分析中药复方红花茯苓提取液对其防治作用。

**方法:** 实验于2003-03/2005-09在广东医学院实验动物中心、药理研究室和中心实验室完成。选用60只SPF级SD大鼠, 随机分为6组, 即正常对照组, 模型对照组, 阳性对照组, 红花茯苓提取液生药0.5 kg/L组, 1 kg/L组, 2 kg/L组, 每组10只, 雌雄各半。红花茯苓提取液3种剂量制剂由广东医学院科技医药开发中心提供, 为红花、茯苓、甘草等中药