

# 山楂、黄芪及刺五加对豚鼠胆固醇代谢的影响

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**内容提要** 本文采用雌性豚鼠随机分组, 分别口服山楂、黄芪及刺五加水煎剂三周, 其肝细胞微粒体及小肠粘膜匀浆羟甲基戊二酰辅酶A还原酶(HMGR)活力明显受到抑制。刺五加对肝细胞微粒体胆固醇 7 $\alpha$ -羟化酶活力有明显的激活作用。这三种中药对正常豚鼠血清总胆固醇及高密度脂蛋白胆固醇的浓度都无明显的影响。并对其原因作了探讨。

高胆固醇血症是动脉粥样硬化的重要诱因, 降低血液中胆固醇的含量, 可使冠心病的发病率大幅度降低<sup>①</sup>。已知具有降血脂作用的中药不少<sup>②</sup>, 但关于它们对胆固醇生物合成的限速酶HMGR及胆固醇分解的限速酶 7 $\alpha$ -羟化酶活力的影响的研究, 国内外尚未见报道。为此, 我们研究了山楂(*Fructus Crataegi*)、黄芪(*Radix Astragali*)以及刺五加(*Acanthopanax senticosus*)对雌性豚鼠肝细胞微粒体 HMGR 活力及 7 $\alpha$ -羟化酶活力, 小肠粘膜HMGR活力, 血清总胆固醇及高密度脂蛋白胆固醇(HDL-C)含量的影响。

## 材料和方法

一、动物: 雌性豚鼠, 体重 350~400g, 随机分组, 每组 8 只。饲养过程中每天12小时亮、暗循环(6:00~18:00, 亮期)。服药三周后于晨 8 时处死取样。

二、药物: 山楂及黄芪由河南医科大学第一附属医院中药房提供; 刺五加为黑龙江齐齐哈尔制药厂生产之刺五加片, 每片含刺五加浸膏 150 mg (批号 840611-5)。用药剂量按成人日服量 (g/kg体重) 折算。均用水煎成浓汁, 使其生药含量相当于: 山楂 0.08g/0.4ml, 黄芪0.1g/0.4ml, 刺五加浸膏15mg/0.4 ml。每只动物每日上午一次喂饲上述药物0.4ml。

三、试剂: DL-3-羟-3-甲基-(3-<sup>14</sup>C)-戊二酰辅酶A(58mCi/mM)为英国Amersham公司产品, (7-<sup>3</sup>H)-胆固醇(26.8Ci/mM)为中国科学院上海原子核研究所产品。DL-3-羟-3-甲基戊二酰辅酶A, 6-磷酸葡萄糖, 6-磷酸葡萄糖脱氢酶, 氧化型辅酶Ⅰ和二巯基苏糖醇均为美国Sigma公司产品。其余均为国产分析纯试剂。

四、测定方法: 肝细胞微粒体HMGR活力测定依照 Erickson 等方法<sup>③</sup>, 略作修改, 以 10N 盐酸代替 10N 氢氧化钠停止酶促反应并促进其产物甲羟戊酸内酯化。采用硅胶G薄层层析分离所生成的甲羟戊酸内酯, 并用液体闪烁计数器测定其比放射活性<sup>④</sup>, 但未加入(5-<sup>3</sup>H)甲羟戊酸内酯作内标准。小肠粘膜匀浆 HMGR 活力测定先采用 Gebhard 等方法<sup>⑤</sup>制备小肠粘膜匀浆, 然后按照 Erickson 等方法测定酶活力。按 Hulcher 等方法<sup>⑥</sup>测定肝细胞微粒体胆固醇 7 $\alpha$ -羟化酶活力。肝细胞微粒体及小肠粘膜匀浆蛋白质含量均按 Lowry 法测定<sup>⑦</sup>。血清总胆固醇及 HDL-ch 含量按杨昌国法<sup>⑧</sup>测定。

## 结 果

山楂、黄芪及刺五加对豚鼠肝细胞微粒体 HMGR 和胆固醇 7 $\alpha$ -羟化酶以及小肠粘膜匀浆 HMGR 活力、

**附表** 山楂、黄芪和刺五加对豚鼠肝及小肠粘膜 HMGR 活力、肝胆固醇 7 $\alpha$ -羟化酶活力和血清胆固醇含量的影响 (M $\pm$ SD)

	动物数	HMGR活力 (pmol/min mg蛋白质)		肝细胞微粒体胆固醇 7 $\alpha$ -羟化酶活力 (pmol/min mg蛋白质)	血清胆固醇含量 (mg/dl)	
		肝细胞微粒体	小肠粘膜匀浆		总胆固醇	HDL-C
对照组	8	25.87 $\pm$ 2.71	40.0 $\pm$ 9.39	13.57 $\pm$ 1.41	44.99 $\pm$ 2.82	12.65 $\pm$ 0.95
山楂组	8	7.94 $\pm$ 1.78*	13.33 $\pm$ 2.05*	9.84 $\pm$ 0.84	47.15 $\pm$ 3.58	9.63 $\pm$ 1.27
黄芪组	8	11.0 $\pm$ 1.75*	15.3 $\pm$ 4.91*	12.37 $\pm$ 1.49	43.95 $\pm$ 3.19	10.09 $\pm$ 0.73
刺五加组	8	18.78 $\pm$ 8.34*	23.61 $\pm$ 4.68*	16.44 $\pm$ 1.93**	44.84 $\pm$ 2.27	12.54 $\pm$ 0.85

注: 与对照组相比 \* P<0.001, \*\* P<0.05;

血清总胆固醇和HDL-C含量的影响,见附表。

从附表可见上述三种中药对肝细胞微粒体和小肠粘膜匀浆HMGR活力均有明显的抑制作用,同时刺五可激活7 $\alpha$ -羟化酶的活力( $P < 0.05$ )。但这些中药对血清总胆固醇和HDL-C的含量均无影响。

## 讨 论

肝脏及小肠粘膜是体内最重要的合成胆固醇之组织<sup>(9)</sup>。豚鼠小肠粘膜若以蛋白质含量计算,其合成胆固醇的速度远远大于肝脏<sup>(10)</sup>。肝脏是唯一能把胆固醇转变成胆酸的器官。HMGR和7 $\alpha$ -羟化酶分别是体内胆固醇合成及分解的限速酶,它们活力的变化分别反映了机体合成和分解胆固醇的状况<sup>(11)</sup>。据此,测定药物对这两种酶活力的影响可得知其对机体胆固醇合成及胆固醇转变成胆酸的作用。上述实验结果证明,豚鼠服用山楂、黄芪及刺五加水煎剂后,对HMGR活力有抑制作用,其中山楂使豚鼠肝细胞微粒体及小肠粘膜的HMGR活力分别下降70%和67%左右,黄芪的作用次之,可使肝脏及小肠粘膜HMGR活力均下降60%左右,刺五加对HMGR活力的抑制作用较弱,分别为28%和41%。但有意义的是,刺五加对肝细胞微粒体7 $\alpha$ -羟化酶的活力有激动作用,可使其活力提高21%,而山楂和黄芪则无此作用。

豚鼠服用山楂、黄芪及刺五加后,对其血清总胆固醇及HDL-C含量无影响。动物服用胆固醇合成的抑制剂或胆固醇分解的激动剂,一般可使其血清胆固醇含量有所下降;本文结果可能因动物种属不同,其对影响因素的反应也不同。例如,CS-514是一种微生物的代谢产物,为鼠肝及肠的HMGR有力的竞争性抑制剂,可以抑制鼠肝细胞白( $^{14}C$ )-醋酸合成胆固醇,但这种物质并不能使大鼠及小鼠血清中胆固醇含量减少,而能使犬、兔和猴血清中胆固醇含量明显下降<sup>(12)</sup>。因此,豚鼠服用山楂、黄芪及刺五加不能使其血清总胆固醇含量下降,可能是因为动物种属不同。详细机

理有待进一步研究。

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## • 简讯 •

▲中国中西医结合研究会广东分会于1987年2月28日在广州市召开第二届理事扩大会议,传达了广东省科协“三大”会议精神;总结了广东分会1986年的工作;布置了1987年工作。广东分会1986年学术活动比较活跃,积极开展医疗咨询工作,受到广东省科协的表彰。  
(罗日永)

▲中国中西医结合研究会湖南分会荣获“先进学会”光荣称号,湖南省科协于1987年3月14日召开了表彰大会,向湖南分会颁发了奖状及奖金,该分会何锐、杨蕴祥、王明辉、郭定九四位同志被评为学会积极分子,并颁发了荣誉证书及奖品。

(湘 讯)

# Effect of "Yiqi Congming" Decoction (益气聪明汤) on the Central Nervous System in Reserpinized Mice

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Experiments showed that many symptoms in chronically reserpinized mice, such as loss of weight, diarrhea, hypothermia, etc., were similar to those of Yang or Qi deficiency syndrome in TCM. These symptoms resulted from the depletion of monoamine transmitters in the brain by reserpine. In order to study the mechanism of central action of Yiqi Congming decoction (replenishing Qi and becoming wise), the effects of the prescription were observed on the contents of norepinephrine (NE) in the hypothalamus, dopamine (DA) in the striatum, 5-hydroxytryptamine (5-HT) and 5-hydroxyindolacetic acid (5-HIAA) in the brainstem of reserpinized mice, and the activity of  $\text{Na}^+ - \text{K}^+ - \text{ATPase}$ ,  $\text{Mg}^{++} - \text{ATPase}$  and mitochondrial ATPase in some districts of the brain, which were closely related to the uptake and the storage of transmitters, and cAMP levels in the brain and the blood of reserpinized mice. The results showed that the content of NE, DA and 5-HT, the activity of  $\text{Na}^+ - \text{K}^+ - \text{ATPase}$ ,  $\text{Mg}^{++} - \text{ATPase}$ , and mitochondrial ATPase and the levels of cAMP were statistically decreased as compared with the control.

After oral administration of Yiqi Congming decoction, NE and DA levels in reserpinized mice increased ( $P < 0.01$ ), while the 5-HT and 5-HIAA contents remained unchanged.

According to the composition of the prescription, four groups were divided to administer the Chinese materia medica. The effect of Qi tonics (*Codonopsis pilosula*, *Astragalus membranaceus* and *Glycyrrhiza uralensis*) were stronger than other drugs. No synergistic effect of Qi tonics and Yang enhancing drugs (*Puerariae lobata*, *Cimicifugae heracleifolia* and *Viticis trifolia*) were observed.

Further study revealed that the activities of  $\text{Na}^+ - \text{K}^+ - \text{ATPase}$  and  $\text{Mg}^{++} - \text{ATPase}$  in some district of brain of reserpinized mice were increased after oral administration of Qi tonics ( $P < 0.05$ ), while only the activity of  $\text{Na}^+ - \text{K}^+ - \text{ATPase}$  was increased after the treatment of Yang enhancing drugs. cAMP levels in the brain (cerebellum not included) and the blood in reserpinized mice were also elevated when Qi tonics were given. The results suggested that Qi tonics may have the pharmacological effects: (1) It maintained activity of  $\text{Na}^+ - \text{K}^+ - \text{ATPase}$  and  $\text{Mg}^{++} - \text{ATPase}$  in the brain to promote uptake of monoamines into the premembranous synapse and the storage granules; (2) It increased cAMP content in the brain to accelerate the synthesis of monoamines.

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# Effect of Sheng Mai Liquor (生脉液) on Hepatic Histochemistry in Aged Rats

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22 healthy aged rats (18 month old) were selected for this experiment. The animals were divided randomly into treated and control groups. These two groups were treated with Sheng Mai Liquor (10 ml/kg per day) and normal saline (10 ml/kg per day) respectively for 3 weeks. The body weight and physical strength were measured before they were sacrificed. The liver was excised and put into the cryostat section and the histochemical reactions with succinate dehydrogenase (SDH), lactate dehydrogenase (LDH), monoamine oxidase (MAO), RNA and glycogen were carried out. The experimental results showed that there was no change on body weight of the aged animals in the treated group, but physical strength were enhanced. The activity of SDH was elevated significantly and the content of RNA and glycogen were increased markedly in the liver of aged rats of treated group than that of the control. But there was no significant difference of hepatic LDH and MAO between these two groups. The results suggest that Sheng Mai Liquor itself may enhance the aged rats' physical strength and promote the functional activity of liver in the aged rats.

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# Effects of *Crataegus pinnatifida*, *Astragalus membranaceus* and *Acanthopanax senticosus* on Cholesterol Metabolism in Guinea Pig

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Crude aqueous extracts of *Crataegus pinnatifida*, *Astragalus membranaceus* and *Acanthopanax senticosus* were given orally to female guinea pigs once daily for three weeks. *Crataegi Pinnatifida* and *Astragalus membranaceus* inhibited the activity of liver microsomal and small intestinal mucosa 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR). *Acanthopanax senticosus* not only inhibited the activity of HMGR, but also enhanced significantly the activity of liver microsomal cholesterol 7 $\alpha$ -hydroxylase. All of the three Chinese drugs showed no evidence of affection on the levels of serum total cholesterol and high density lipoprotein cholesterol (HDL-C), the cause of which has been explored.

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