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薤白提取物胶丸防治动脉粥样硬化的临床观察

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内容提要 132例高脂血症患者口服薤白提取物胶丸4周后，比较服药前后血浆总胆固醇、β脂蛋白、血浆6-酮-前列腺素$F_{1\alpha}$的变化，P值均<0.001；血小板聚集率服药前后对比P<0.01，表明该药有降低血脂、提高6-酮-前列腺素$F_{1\alpha}$水平、抑制血小板聚集的作用，为防治动脉粥样硬化提供了一个有效的新型药物。

薤白(*A nerinifolium* Bak)为民间广泛食用的野菜，医书记载其有散瘀血等作用。我校药物研究室对其有效成分进行了提取，为长梗薤白提取物(简称ANBE)，并制成胶丸。我科于1983年开始应用于高脂血症患者，现将观察结果报告如下。

资料与方法

一、病例选择：选择住院患者74例，门诊患者58例，共132例。男82例，女50例，年龄30～74岁，平均53岁。全部患者均为原发性高脂血症，经3次检查血浆总胆固醇(TC)≥250 mg/dl，甘油三酯(TG)≥160 mg/dl，β脂蛋白(胆固醇折算法)≥450mg/dl，其中1项以上异常者即列在本实验组。

二、实验方法：观察期间患者停服其它降脂及抑制血小板聚集的药物，饮食如常。药物采用我校药物研究室提供的ANBE，每丸0.25g(相当于生药6.1g)，每次服2丸，1日3次口服，服药4周为1个疗程，1个疗程后评定疗效。

三、观察指标：服药前后分别取静脉血测定TC、TG、β脂蛋白和6-酮-前列腺素$F_{1\alpha}$，严格控制采血和实验室条件，采血后同批平行测定，放免药箱由解放军总医院提供。血小板聚集率测定使用北京生化仪器厂生产的血小板聚集仪，用ADP作诱导(西德Baehriqer mannheim Gm 6H产品)。所得结果用t检验法进行显著性检验。

结 果

一、132例患者治疗前后血脂的变化：见附表。

附表 132例患者治疗前后血脂(mg/dl)变化对比 (M±SD)

	TC	TG	β脂蛋白
治前	262.9±56.4	162.7±87.1	421.9±114.2
治后	197.7±51.4	141.3±37.3	334.5±110.0
t	4.02	1.85	7.58
P	<0.001	>0.05	<0.001

结果表明口服ANBE对高脂血症患者有明显的降低血浆β脂蛋白和TC的作用(P均<0.001)，对降低TG也有较好的效果，但不如前两者显著。

二、血浆6-酮-前列腺素$F_{1\alpha}$的变化：本组治疗前测定21例患者血浆6-酮-前列腺素$F_{1\alpha}$为1296.95±106 pg/ml(M±SD，下同)，服药后17例复查，有明显升高，为3271.12±579 pg/ml，治疗前后对比t=6.8，P<0.001，差

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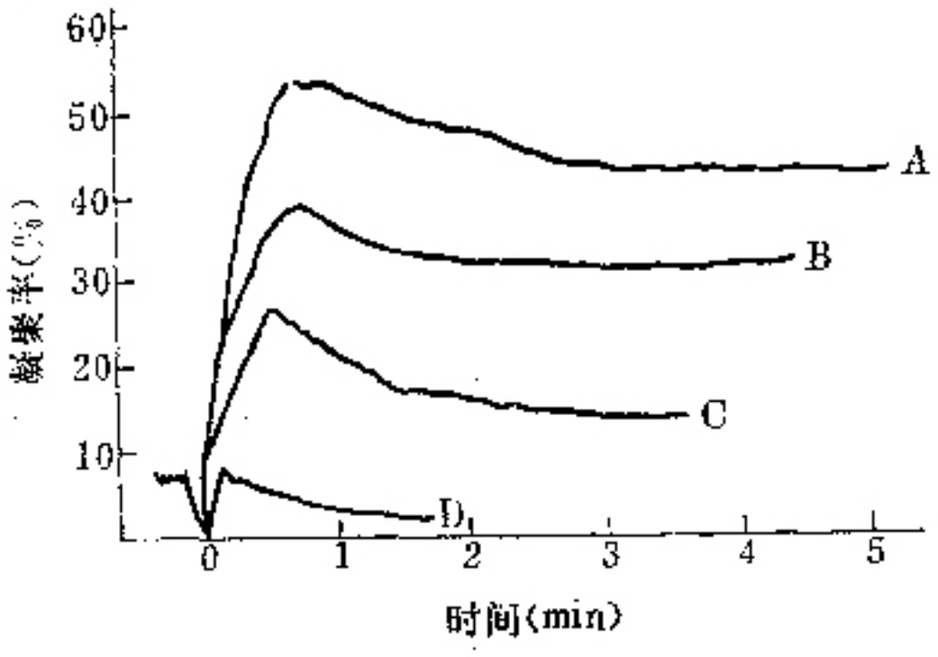
异有非常显著性意义。

三，对血小板聚集率的抑制作用：本组资料齐全的 8 例进行治疗前后血小板聚集曲线高度(mm)比较（见附图），并计算给药后血小板聚集抑制的百分率。结果治疗前后血小板聚集率(M±SD)分别为 51.56±25.35、26.85±16.79，治疗前后对比，t=3.49，P<0.01，差异有非常显著性意义。治疗后平均抑聚率 47.36%。



附图　血小板聚集率曲线

A：治疗前平均聚集率曲线；B：治疗后降低最小聚集率曲线；C：治疗后降低平均聚集率曲线；D：治疗后降低最大聚集率曲线

讨　论

一、血管内膜中脂质沉积是动脉粥样硬化病变发生的始动环节，因而处理高脂血症是防治动脉粥样硬化的重要措施。本组实验证明 ANBE 有降血脂作用。已研究证实 ANBE 中含有甲基烯丙基二硫和甲基烯丙基三硫及其它含硫化合物[1]，可能是 ANBE 降血脂的有效成分。ANBE有升高前列腺素I_2(PGI_2)的作用，从而升高细胞内 cAMP 水平[2]，其结果促进平滑肌细胞内酸性胆固醇酯水解酶活性，促进胆固醇酯的水解和转运[3]，ANBE 的降血脂作用机理，有待进一步深入探讨。

二、ANBE 胶丸有提高高脂血症患者血浆 6-酮-前列腺素 $F_{1\alpha}$的作用，6-酮-前列腺素 $F_{1\alpha}$ 是 PGI_2 的非酶水解产物，性质稳定，因而测定其含量可以反映 PGI_2 的含量[4]。我校病理教研室研究证明，ANBE 对于用高胆固醇饲养动物模型有升高实验动物 PGI_2 水平的作用。高血脂时血清过氧化脂质(LPO)升高[5]，现已知 LPO 有选择性抑制 PGI_2 合成酶，使 PGI_2 合成减少。ANBE 有明显降低血清和动脉壁中的 LPO 的作用，从而使内皮细胞及平滑肌细胞的 PGI_2 合成酶得到保护，从而升高了 PGI_2 的含量，减轻动脉粥样硬化的病变。

三、本组提示 ANBE 有抑制高脂血症患者血小板聚集的作用，有人在动物实验中观察到 ANBE 有较强的抑制血小板聚集作用，同时还有解聚作用[1,2]。因此认为口服 ANBE 可以防治动脉粥样硬化的形成，为防治动脉粥样硬化提供了一个有效的新型药物。本品无毒，可以长期服用，且使用方便，易被患者接受。

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Abstracts of Original Articles

Effects of Sodium Ferulate on Platelet Aggregation and Platelet TXA_2 in Patients with Coronary Heart Disease

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Sodium ferulate (SF), one of the active principles of *Angelica sinensis*, was investigated in vitro and in vivo for its anti-platelet effects. In vitro, SF inhibited platelet aggregation was induced by epinephrine or ADP as well as inhibited platelet TXB_2 (a metabolite of TXA_2) generation, which occurred in the platelet rich plasma of patients with CHD, in a dose dependent fashion. At low concentration, SF showed a markedly inhibitory effect on platelet TXB_2 generation more than that on platelet aggregation. While at a higher concentration, platelet aggregation was more evidently suppressed than platelet TXB_2 generation. The results suggest that SF, in vitro, could effectively inhibit the platelet aggregation in patients with CHD, which was partly related to the inhibition of TXA_2 generation. SF was also intravenously infused, in a dosage of 4 mg/kg. However, both 6-keto-$PGF_{1\alpha}$ and TXB_2 in plasma and in serum remained unchanged; platelet aggregation and platelet TXB_2 generation were lower than the values measured before SF infusion, but, as compared with placebo, no significant difference statistically was observed. Inadequate dosage might be the main cause for the failure.

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Clinical Observation on Anti-Atherosclerosis Effect with *Allium nerimifolium* Extract Capsule

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Allium nerimifolium (AN) is a kind of wild vegetable widely taken for food in the countryside. It was recorded in TCM books that it was treated in relieving chest pain. The active principles of AN have been isolated. One of these principles, methylallyl compound, is an effective agent in inhibiting platelet aggregation and prouducing thromboxane A_2 (TXA_2). Recent data showed that AN contains prostaglandin A_1 (PGA_1). The AN capsule is the extract of AN supplied by the pharmaceutical department of our university. The capsule has been used in our hospital for more than three years. The criteria for diagnosis of primary hyperlipidemia were: plasma total cholesterol (TC) 250mg/dl, trinitroglycerin (TG) ≥160 mg/dl and β-lipoprotein (β-LP) ≥450 mg/dl, any one of the above items reached these values, and hyperlipidemia could be diagnosed. 0.5 mg of AN per os, 3 times a day was given to 132 patients with hyperlipidemia for 4 weeks. During this period, no other drugs inhibiting platelet aggregation or decreasing plasma lipid were administered, and all of the patients were allowed to take their ordinary food as usual. Plasma lipid, 6-keto-prostaglandin $F_{1\alpha}$ (6-k-$PGF_{1\alpha}$) and platelet aggregation (PAg) were measured before and after the treatment. The main results were as follows: before administration the average of TC, TG, β-LP and 6-k-$PGF_{1\alpha}$ were 262.9±56.4, 162.7±87.1, 421.9±114.2 and 1296.95±106 pg/ml respectively, and after medication 197.7±51.4, 141.3±37.3, 334.5±110.0 and 3271.12±579 pg/ml respectively. Platelet aggregation assay was performed in 8 out of 132 cases. PAg values were 51.56±25 and 26.85±16 respectively before and after treatment. The average inhibition rate was 47.36%. The results showed that administration of AN capsule could lower the levels of plasma TC, TG, β-LP and elevate the level of 6-k-$PGF_{1\alpha}$, $P < 0.01$. It also inhibited PAg at the same time. It is well known that hyperlipidemia and hypercoagulable state of the blood are very important pathogenetic factors of atherosclerosis, while 6-k-$PGF_{1\alpha}$, a stable metabolic product prostaglandin I_2 (PGI_2), is an effective platelet aggregation inhibiting agent and also a potent coronary artery dilating agent. It is concluded that the AN capsule is obviously effective in preventing the pathogenesis of atherosclerosis.

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