EFFECT OF KOREAN RED GINSENG ON EICOSANOID BIOSYNTHESIS IN PLATELETS AND VASCULAR SMOOTH MUSCLE CELLS

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INTRODUCTION

Platelet hyperfunction such as enhanced platelet aggregability associated with overproduction of TXA_2, a potent anti - platelet aggregatory and vasoconstrictive substance, has been frequently encountered in patients with cerebral and cardiovascular thrombotic diseases. Prostacycline (PGI_2), a potent anti - platelet aggregatory and vasodilatatory substance produced in vascular walls, also has been reported to be less synthesized in patients with atherosclerotic changes than normal subjects.

We previously described that oral administration of ginsenoside Rg_1(G - Rg_1) or G - Rg_3, main components of Korean Red Ginsengs (KRGs) has a potent anti - platelet aggregatory action. Thus KRGs may have anti - thrombotic effect and thereby may be useful for prevention and treatment of atherosclerotic and thrombotic disorders.

Accordingly the present investigations were performed to study the effect of KRGs on eicosanoid biosynthesis in platelet and vascular walls in order to elucidate further in detail the anti - thrombotic action of KRGs.

STUDY OF GINSENG SAPONIN ON EICOSANOID BIOSYNTHESIS AND AGGREGABILITY OF PLATELETS

We previously reported that in vitro study among various ginseng saponins, only G - Rg_1 and G - Rg_3 had a potent suppressive effect on platelet aggregation stimulated by various aggregants such as collagen, ADP, epinephrine and arachidonic acid (AA). Also G - Rg_1 inhibited 9, 11 - epithio - 11, 12 - methano - TXA_2(stable TXA_2 ; $STXA_2$) - induced platelet aggregation, while the specific binding of [^{3}H]SQ29548.(specific TXA_2 receptor antagonist) to human platelet was not affected. Agents which increases cAMP and c GMP levels in platelets have been described to inhibit platelet aggregation. So we investigated the effect of G - Rg_1 on the basal levels of these two cyclic nucleotides in washed platelets. G - Rg_1 had no effect on the basal levels of cAMP and cGMP. Therefore this possibility seems to be less likely. Interesting finding is that when measured by Quin 2, an increase of cytosolic Ca^{++} in platelets stimulated by $STXA_2$ was dose dependently decreased by in vitro addition of G - Rg_1 with resultant decrease of platelet aggregation.

2.7 g/day of KRGs was orally administered to 10 patients with cerebro - and cardiovasular thrombotic diseases for 4 weeks. Platelet aggregability induced by collagen or V46619(one of the $STXA_2$) was significantly suppressed with a concomitant decrease of TXA_2 production. On the basis of these results obtained by the in vitro and in vivo experiments, it is our thought that G - Rg_1 or G - Rg_3 may exert its anti - platelet aggregatory action by decreasing TXA_2 formation in platelets most likely by inhibiting Ca^{++} influx.

Urinary excretion of 11 - dehydro - thromboxane B_2 (11 - dehydro TXB_2), one of the major metabolites of TXA_2 and 2, 3 - dinor - 6 - Keto - $PGF_{1\alpha}$, one of the major metabolites of PGI_2 were determined in 20 patients with various cardiovascular thrombotic disorders after 4 weeks of oral ingestion of 2.7 g/day of KRGs.

Collagen or ADP - induced platelet aggregation was significantly decreased. On the other hand, urinary excretion of 2, 3 - dinor - 6 - Keto - $PGF_{1\alpha}$ was significantly increased, while that of 11 - dehydro - TXB_2 was unchanged. Therefore the ratio of 2, 3 - dinor - 6 - Keto - $PGF_{1\alpha}$ to 11 - dehydro - TXB_2 (PGI_2 - M/TXA_2 - M) was significantly increased after 4 week administration of KRGs.

STUDY OF PGI_2 PRODUCTION IN VASCULAR SMOOTH MUSCLE CELLS

In cultured smooth muscle cells obtained by rat thoracic aorta, conversion of ^{14}C - AA to ^{14}C - 6 - Keto - $PGF_{1\alpha}$ was determined after co - incubation with various ginsenosides. Interestingly only by addition of G - Rc, enhanced conversion of ^{14}C - AA to ^{14}C - 6 - Keto - $PGF_{1\alpha}$ was noted. On the other hand, conversion of ^{14}C - PGH_2 to ^{14}C - 6 - Keto - $PGF_{1\alpha}$ was unchanged. Northern blot analysis of total RNA prepared from vascular smooth muscle cells showed that in vitro addition of G - Rc increased mRNA level of cyclooxygenase in smooth muscle cells. These results indicate that the enhanced PGI_2 formation by G - Rc could be partly ascribed to an increased cyclooxygenase activity and that G - Rc stimulated gene expression of cyclooxygenase in G - Rc treated vascular smooth muscle cells.

SUMMARY

From in vivo and in vitro experiments using Korean Red Ginseng and its main components, ginsenoside saponins, it was found that ginsenoside may exerts its anti - thrombotic action by decreasing TXA_2 formation in platelets and increasing PGI_2 formation in vascular walls. This may certainly contribute to prevention and development of atherosclerosis and thrombosis by administration of Korean Red Ginsengs.