SOME ASPECTS OF MOLECULAR MECHANISM OF KOREAN RED GINSENG ACTION

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Dear colleagues, Ladies and Gentlemen !

It is well known, that ginseng has been utilized for more than five thousand years in China and is now popular in the world. From ancient times ginseng has been used for the prevention and treatment of a variety of pathological conditions, particularly associated with aging. Ginseng used as a healthful tonic stimulant and having so-called adaptogenic effect, increases nonspecific resistance of the body. It is interesting to note, that since about the tenth century A.D. the red ginseng has been manufactured in Korea and exported to other countries. At present Korea Ginseng and Tobacco Research Institute is the greatest scientific center for manufacturing of Korean red ginseng and investigation of its mechanism of action. It should be noted that many aspects of mechanism of ginseng action is not yet elucidated.

Ginseng root by its chemical composition is really a drug store, but during the isolation of its constituents their activity is significantly decreased. Although many constituents of ginseng can become independent drugs, our opinion is that ginseng is made by nature for application wholly without any separation of its constituents.

During our investigation we used so-called "water" extract of Korean red ginseng roots which was made from ethyl alcohol extract after removing of alcohol by rotatory evaporator in low temperature. In literature there is indication, that ginseng roots stimulated the energetic processes, but there is no detail investigation of this problem. In this point of view it was interesting to study the influence of ginseng preparation on energy supply of different organs. In our first investigation we have showed that ginseng has no any effect on oxygen consumption by brain whole tissue without its fractionation. Further investigations have shown that ginseng significantly enhances oxygen consumption by brain mitochondrial fraction. As you can see from Fig. 1, depending on the amount of preparation used the oxygen consumption by rat brain mitochondria increases from 17% to 31%. This is control and those are after giving ginseng preparation. From this slide you may see that maximal effect was found from 25 mg original root weight in 1 ml incubation medium.

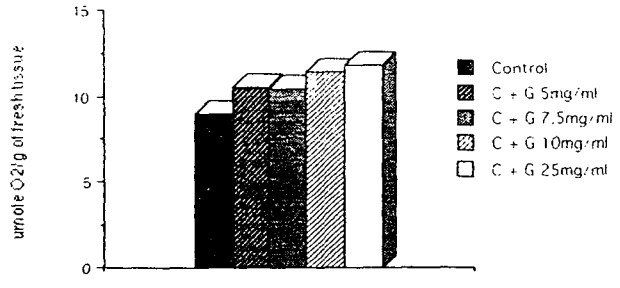

Fig. 1. Influence of Korean red ginseng on oxygen consumption by rat brain mitochondrial fraction.

In the second slide it is shown the influence of ginseng preparation on oxygen consumption by rat liver mitochondrial fraction. You can see that comparatively small amount of ginseng (7.5mg/ml) stimulated this process much more in liver than in brain mitochondria. In the case of liver the stimulation is by 58.9%, while in the case of brain it is only by 15.8%.

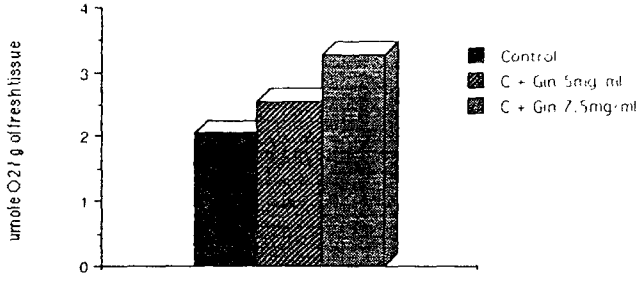

Fig. 2. Influence of Korean red ginseng on oxygen consumption by rat liver mitochondrial fraction.

In the slide 3, it is represented the result of the influence of ginseng on the oxygen consumption by heart mitochondrial fraction. In this case also ginseng significantly enhances oxygen consumption by mitochondrial fraction. Data obtained show that the highest effect from ginseng was found in liver mitochondrial fraction and less in brain mitochondria. So, we have obtained data, showing that one of the mechanisms of ginseng action is the stimulation of energy supply in different organs and systems of body which is expressed in the increase of oxygen consumption by organism.

Every day regularly people undergo action of surrounding factors, including different kinds of stress factors. During a weak intensity of stress factors the organism is able to adaptation. During the action of strong stress factors and the increase of their prolongation the organism is not able to adaptation, and there appears different kinds of diseases, particularly diseases of nervous system. In this case arises a necessity to look for antistressor remedies. In the formation of stress syndrome it

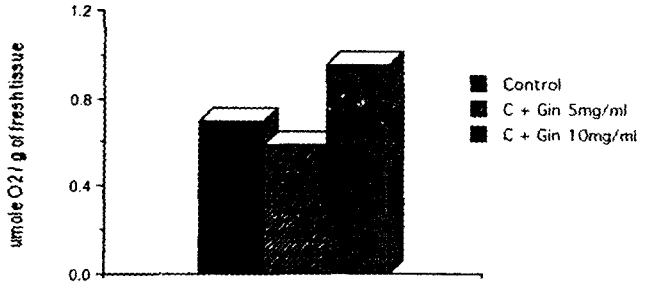

Fig. 3. Influence of Korean red ginseng on oxygen consumption by rat heart mitochondrial fraction.

plays an important role the activation of sympatho - adrenal system, the increase of function of brain cortex, hypothalamus, adrenal glands, owing to the increase of epinephrine and corticosteroids production which activate the function of different organs and systems.

One of the main characteristics of the stress syndrome is the intensification of lipid peroxidation, the increase of free radicals which make their destructive effect on organism. From this point of view the attempting to find an antistressor remedy, so - called adaptogen for increasing nonspecific resistance of organism, is one of the main problems of contemporary biology and medicine. Such compounds are ginseng, eleuterococcus, vitamine E, and generally, antioxidants. I must tell you, that we have prepared substance "S" of plant origin, which have ginseng like properties and significantly prolongs the life span and has antioxidant effect. On the other hand the antioxidant also increase the life span.

Data of Fig. 4. show that during the immobilization stress the nonenzymatic and enzymatic lipid peroxidation in rat brain microsomes increases correspondingly by about 28% and 23%. In stressed animals ginseng decreases brain microsomes nonenzymatic lipid peroxidation by 47.3% and has a small decreasing effect on enzymatic lipid peroxidation (9.2%). As you can see ginseng has no any effect on lipid peroxidation in intact(not stressed) animals.

In the slide 5, there are represented the changes of lipid peroxidation in rat liver microsomes during ginseng administration. In this case the nonenzymatic and enzymatic lipid peroxidation in stressed animals decreases correspondingly by 34.2% and only 9.3%.

Under this experimental condition superoxide dismutase activity (see Fig. 6.) which destroy superoxide radicals in liver preparation increases by 55.5%, but the changes of this activity in brain tissue is less significant. In our opinion ginseng on the one hand prevented increasing of the lipid peroxidation levels and on the other hand increases the destruction of superoxide radicals. This effect is one of the main mechanisms of ginseng action.

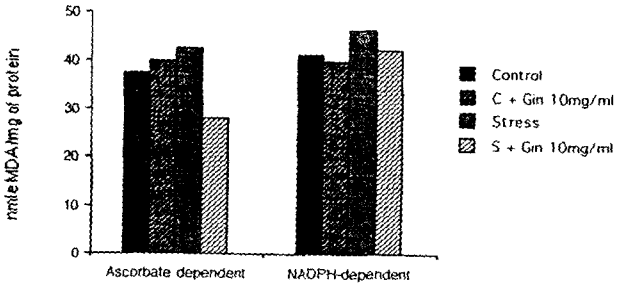

Fig. 5. Influence of Korean red ginseng on lipid peroxidation in rat liver microsomes.

At present it is well known that the enzyme gammaglutamyltransferase, which has important role in amino acids, particularly neuromediatory amino acids transport by increasing its activity under different pathological conditions. Perhaps, it is possible by this way to explain the universal changes of cell and other membranes. Our investigation shows that ginseng has no any effect on brain synaptosomal gammaglutamyltransferase in intact animals. In our early investigation we have shown that ginseng - like compounds expressed the effect on this enzyme only after inhibition of enzyme activity by specific inhibitors, for example by ethyl alcohol, or N - acetyl - L - aspartic acid(our findings), which is a brain specific compound.

Data from Fig. 7. show that N - acetyl - L - aspartic acid strongly inhibited common gammaglutamyltransferase activity (GGT) of brain synaptosomal fraction. Under this condition ginseng has no effect on enzyme activity. We found the absence

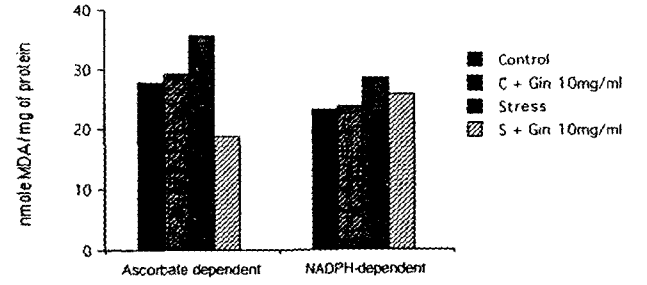

Fig. 4. Influence of Korean red ginseng on lipid peroxidation in rat brain microsomes.

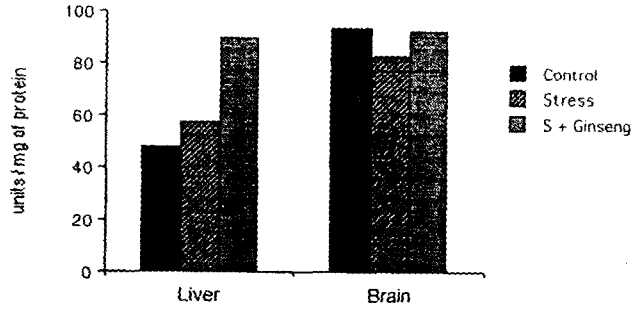

Fig. 6. Influence of Korean red ginseng on superoxide dismutase activity in rat brain and liver.

of ginseng effect during working with slightly bounded enzyme. Fig. 7. indicates that the activity of tightly bounded GGT in comparison with slightly bounded enzyme is very high. Activity of this type of enzyme is also strongly inhibited by NAA. In this case ginseng increases the enzyme activity by five times, So, our findings show that ginseng has regulatory effect on GGT activity. Our findings show that in certain experimental conditions ginseng can be used for regulation of GGT activity and by this way can transport the amino acids across the cell and other membranes.

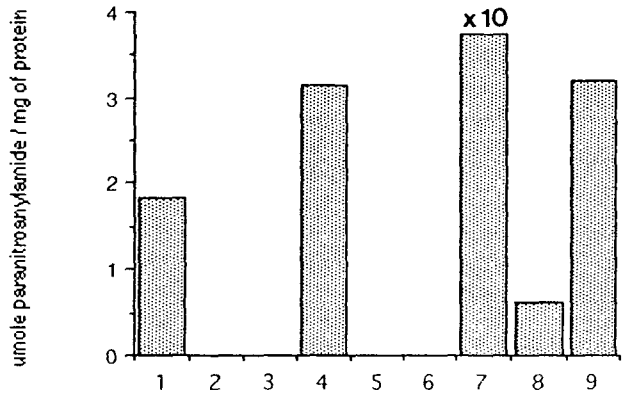

Fig. 7. Influence of Korean red ginseng on gammaylutamyltransferase activity of brain synaptosomal fraction.

From this point of view it is very interesting results of our investigation with connection of significance of ginseng in neurotransmitter amino acid transport processes, their uptake, release and binding with amino acid receptor systems. Data represented in Fig. 8. show, that ginseng in concentration 10 and 15 ㎎ of original root weight/㎖ incubation medium strongly increases K^+ - evoked release of excitatory neuromediator ^{14}C - glutamic acid from rat brain synaptosomes. We suggest that in mechanism of stimulatory and tonic effect of ginseng plays an important role stimulation of excitatory neuromediator glutamic acid release in synaptic cleft and hence interaction of neuromediator with its postsynaptic receptor.

Findings show new aspects for ginseng action mechanism investigation. Thank you.

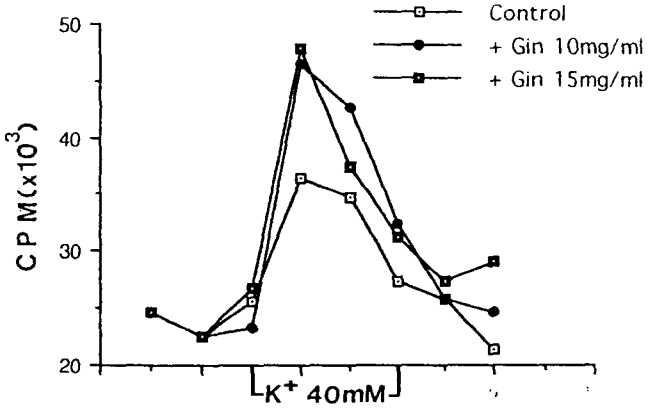

Fig. 8. Influence of Korean red ginseng on K^+ - evoked release of ^{14}C - glu from rat byain synaptosomes.