Effect of Panax ginseng on andropausal disturbance

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We have previously reported that administration of Korean red ginseng water extract (KRG-WE) protects the testis against 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced damage in guinea pigs. The first experiment was carried out to investigate histopathologically the beneficial role of KRE-WE (*i.p.*) on guinea pig testis damaged by TCDD. Ninety guinea pigs were divided into six equal groups. The normal controls (group 1) received vehicle and saline; group 2 received TCDD(1 μg/kg) intraperitoneally; group 3 and 4 received 100 or 200 mg/kg per day of *Panax ginseng* water extract (PG-WE) intraperitoneally for 28 days from 1 week before TCDD injection; groups 5 and 6 received PG-WE for 14 days from 1 week after TCDD treatment. The gain in body weight was less in groups treated with TCDD than in controls. Moreover, the body weight of groups 2 decreased from 14 days after TCDD exposure, while that of groups 3 and 4 increased; there was no decrease in body weight in groups 3-6. The decrease in testicular weight caused by TCDD was prevented by PG-WE. Light microscopy showed smaller tubules and late maturation arrest in group 2; electron microscopy showed a dissolution of the germinal epithelium, disrupted tight junctions between adjacent Sertoli cells, and altered germ cells at all developmental stages. The maturation arrest in germ cells caused by TCDD was ameliorated in groups 3-6. The testes almost completely recovered in groups 3 and 4 and there was some therapeutic effect of PG-WE in groups 5 and 6. These results confirm the protective and therapeutic effects of *Panax ginseng* on atrophy and testicular damage induced by TCDD, providing evidence that ginseng might be a useful agent in preventing and treating testicular damage induced by environmental pollutants.

The second experiment was carried out both to verify the beneficial role of *Panax ginseng* (*p.o.*) in rats and elucidate active ingredients that could protect the testis from TCDD-induced toxicity. Korean red ginseng crude saponine (KRG-CS) was prepared by Diaion HP-20 adsorption chromatography. One hundred twenty rats (Sprauge Dawley, 200±10 g) were divided into 6 groups. The normal control group (NC) received vehicle (i.p.) and saline (p.o.). Predetermined dose of

TCDD (40 μg/kg b.w., *i.p.*) was administered to single TCDD-treated (TT) and test (CS) groups. KRG-CS was administered (p.o.) at daily doses of 5 (CS5), 10 (CS10), 20 (CS20) and/or 40 mg/kg b.w. (CS40) for 5 weeks, starting 1 week before the TCDD-exposure. Body weight gain, organ weights, and sperm quality were investigated. Decrease in body weight gain induced by TCDD was greatly attenuated by KRG-CS in a dose-dependent manner. Testicular weight, sperm head counts and ratio of sperm with progressive movement in TT group decreased significantly but those parameters were improved by the treatment of KRG-CS in a dose-dependent manner. This result led us to conclude that crude saponin might be the active ingredient of Korean red ginseng that attenuates the testicular toxicity induced by TCDD.

The third experiment was performed to further assess the effect of *Panax ginseng* on survival and sperm quality of guinea pigs exposed to TCDD. Eighty male guinea pigs were divided into eight equal groups. The normal control (NC) group received vehicle and saline; one dose of 1 μg/kg body weight TCDD was injected intraperitoneally into the single TCDD-treated (TT) and test groups (P100, P200, C100, C200); G and NC groups received vehicle instead of TCDD. P. ginseng water extract (PG-WE) was injected intraperitoneally at daily doses of 100 (G100, P100, C100) or 200 mg/kg body weight (G200, P200, C200). The PG-WE was administered to the P and G groups for 12 weeks from 1 week before TCDD exposure, and to the C groups for 10 weeks from 1 week after TCDD exposure. After a 4-week discontinuation of PG-WE treatment after the 13th week the surviving males were then tested for fertility by mating them with females. The litter size, death rate, male/female birth ratio and physical abnormalities of the progeny were investigated. After confirming delivery of the offspring, the parent males were killed at 40 weeks, their testes weighed and sperm quality assessed. All TT animals died within 18 days after TCDD exposure, but 40-70% of the PG-WE-treated groups, depending on the groups, survived until death at 40 weeks. All the surviving males were fertile regardless of TCDD exposure; there was no difference in litter size between the NC and test groups. Notably the death rate of progeny born to PG-WE-treated groups was lower than that of progeny born to TCDD-exposed groups (P200 and C groups). The progeny born to TCDD-esposed groups (P200 and C groups) had a preponderance of females. G Group animals had higher sperm quality than that of NCs even long after discontinuing PG-WE.

Most recently, we performed an animal experiment to elucidate the biological role of Korean red ginseng on senile testicular dysfunction and compare the efficacy between KRG-WE and its crude saponin fraction (CS). A total of 24 male rats (Sprague-Dawley), consisting of eighteen 12-month-old (6 heads/group) and six 2-month-old, were employed for the experiment. They were kept in Konkuk RIC animal rearing SPF facility and the animal experiment was carried out in accordance with the Institutional Animal Care and Use Committee Guidelines of Konkuk University. The old control (OC) and young control (YC) groups received solid food and water *ad libitum.* KRG-WE and CS groups received Korean red ginseng water extract and its crude saponin fraction at daily doses of 200 mg/kg b.w. and 40 mg/kg b.w., respectively for four months. In general, Korean red ginseng and its saponin fraction attenuated aging-related abnormal increase in AST, ALT, γ-GTP and BUN levels significantly ($p<0.05$). Motility, progressiveness and curvilinear velocity (VCL) of sperm in ginseng-

treated group showed significant improvement in comparison with those of OC ($p<0.05$). It was evident that average path velocity (VAP) and straight line velocity (VSL) were also improved but demonstrated no significant difference due to too wide variation. There was no significant difference in percent of tubule with sperm between young and old rats. However, sperm counts per tubule, SCI and Johnsen's score decreased significantly depending on aging ($p<0.05$). Other spermatogenesis-related parameters were also decreased by aging but demonstrated no significance. On the other hand, it was apparent that administration of ginseng improved spermatogenesis-associated parameters compared with OC. Serum testosterone level was not decreased but FSH and LH levels increased markedly by aging. It was interesting to note that ginseng elevated testosterone level but decreased abnormal increase in FSH and LH levels in old rats. Cross section of seminiferous tubules showed remarkable difference between young and old rats. Ginseng demonstrated distinct testicular histological improvement in old rats. From these results, we could assumed that saponin fraction was the active ingredient of *Panax ginseng*. However, overall data demonstrated that KRG-WE was more effective than saponin fraction.

In conclusion, Korean red ginseng improves and/or protects testicular dysfunction significantly no matter how the dysfunction comes from aging or environmental pollutants. In addition, it would be most probable that saponin fraction is the active ingredient of *Panax ginseng*. However, it is apparent that total water extract is more effective than its corresponding saponin fraction.