

## Research Article

# Effect of Brain-Cor Injection of Ginkgo on the Hyperlipemia and Thrombosis: Fundamental Study

**Hong YC\*, Jo KH and So CH**

Department of Obstetrics and Gynecology, Pyongyang University of Medical Sciences, Democratic People's Republic of Korea

**\*Corresponding author:** Hong YC, Department of Obstetrics and Gynecology, Pyongyang University of Medical Sciences, Democratic People's Republic of Korea**Received:** August 20, 2021; **Accepted:** September 17, 2021; **Published:** September 24, 2021**Abstract**

We have done this study to verify effects on the serum lipid content (TC, TG, HDL-C) in experimental model of hyperlipemia and on the blood coagulability in experimental model of thrombosis.

**Background:** Female hormone preparation is limited in long term use because of hyperlipemia and thrombosis that are complications occurring in long term use of female hormone preparations for dysfunctional uterine bleeding, climacteric disorder, female genital organs tumor. Therefore to prevent complications such as hyperlipemia and thrombosis with female hormone preparation use are the acute problems not only for the effective treatment of gynecological diseases but also for the lowering of incidence rate of hypertension, arteriosclerosis, hyperlipemia and thrombosis.

We made brain-cor injection of Ginkgo for the treatment of hyperlipemia and thrombosis that are complications occurring in long term use of female hormone preparations and verified its effects on the serum lipid content in experimental model of hyperlipemia and on the blood coagulability in experimental model of thrombosis.

**Objects and Materials:** Wistar rats with 160~180 g in body weight were used as experimental animals, brain-cor injection of Ginkgo(70mg/20mL) made from Ginkgo extract that consists of flavonoid content above 24%, total lactone content above 6% and total ginkgolic acid content below 5µg/g was used as drugs.

**Methods:** For 15 days brain-cor injection of Ginkgo 10mg/kg was injected in abdominal cavity of experimental model of hyperlipemia by tween-80, serum was separated from collected blood in orvita vein, serum TC (Total Cholesterol) content, serum TG (Triglyceride) content and serum HDL-C (High Density Lipoprotein-Cholesterol) content were examined with blood automatic biochemical analyzer and measurements were compared each other. For 15 days brain-cor injection of Ginkgo 10mg/kg was injected in abdominal cavity of experimental model of hyperlipemia and thromboplastin 0.5% 0.1mL/10g was injected on cauda vein in an hour after the last injection of Ginkgo. BT (Bleeding Time), CT (Clotting Time), APTT (Activated Partial Thromboplastin Time) and PT (Prothrombin Time) were examined and measurements were compared each other.

**Results:** Brain-cor injection of Ginkgo decreased serum TC and TG content and increased serum HDL-C content in experimental model of hyperlipemia. And brain-cor injection of Ginkgo prolonged BT, CT, APTT and PT significantly in experimental model of thrombosis.

**Keywords:** Female hormone preparation; Hyperlipemia; Thrombosis; Brain-cor injection of Ginkgo

**Abbreviations**

TC: Total Cholesterol; TG: Triglyceride; HDL-C: High Density Lipoprotein-Cholesterol; BT: Bleeding Time; CT: Clotting Time; APTT: Activated Partial Thromboplastin Time; PT: Prothrombin Time

**Introduction**

Up to now a lot of studies for the treatment of disease with ginkgo leaves have been progressed and in the process of study medicines and

healthy food such as Ginkgo pills for arteriosclerosis, cor injection of Ginkgo, cor tincture of Ginkgo and Ginkgo tea were standardized and used. But these medicines and healthy food were prepared from Ginkgo extract with only flavonoid content above 24%, but not lactone components, therefore they do not display enough therapeutic effect.

Worldwide standardized and used Ginkgo extract consists of flavonoid content above 24%, total lactone content above 6% and total ginkgolic acid content below 5µg/g. This Ginkgo extract is acknowledged as natural medicine that is effective in the treatment

of cardiovascular and nervous system diseases such as cerebral apoplexy, angina pectoris, hypertension, hyperlipemia, senile dementia, diabetes mellitus and has few side effects. Especially it is known that lactone component in Ginkgo extract is a strong natural inhibitor to platelet-activating factors. At present Ginkgo preparation is developing into one of the medicines in high demand in the treatment of cardiovascular and nervous system diseases.

On the other hand female hormone preparation is limited in long term use because of hyperlipemia and thrombosis that are complications occurring in long term use of female hormone preparations for dysfunctional uterine bleeding, climacteric disorder, female genital organs tumor. Therefore to prevent complications such as hyperlipemia and thrombosis with female hormone preparation use is becoming an acute problem not only for the effective treatment of gynecological diseases but also for the lowering of incidence rate of hypertension, arteriosclerosis, hyperlipemia and thrombosis.

## Objects and Methods

### Objects

Wistar rats with 160~180 g in body weight were used as experimental animals.

### Materials

Brain-cor injection of Ginkgo (70mg/20mL) made from Ginkgo extract that consist of flavonoid content above 24%, total lactone content above 6% and total ginkgolic acid content below 5 $\mu$ g/g was used as drugs for study group, and cor injection of Ginkgo made from Ginkgo extract with only flavonoid was used as drugs for control group.

### Methods

**Methods to examine the effect of brain-cor injection of Ginkgo on serum TC, TG and HDL-C content:** Experimental model of hyperlipemia (control group) was made by injection of tween-80 1g/kg in abdominal cavity of rat five times every other day. Study group No 1 was administrated cor injection of Ginkgo (control drug) and study group No 2 was administrated brain-cor injection of Ginkgo (study drug). Study groups were administrated injections 10mg/kg in abdominal cavity for 15 days. Normal group were not administrated any drugs. Serum was separated from collected blood in orvita vein, serum TC(total cholesterol) content, serum TG (Triglyceride) content and serum HDL-C (high density lipoprotein-cholesterol) content were examined with blood automatic biochemical analyzer, and measurements were compared each other.

**Methods to examine the effect of brain-cor injection of Ginkgo on blood coagulability:** Cor injection of Ginkgo and brain-cor injection of Ginkgo were injected 10mg/kg in dose for 15 days in abdominal cavity of experimental model belonging to the study group

No 1 and No 2 respectively, thromboplastin 0.5% 0.1mL/10g was injected on cauda vein in an hour after the last injection of Ginkgo. Control group was injected only thromboplastin and normal group was not administrated any drugs. Some parameters for coagulation were examined and compared each other. BT (Bleeding Time) was examined by Duke method, CT (Clotting Time) was examined by Zali-Ponio method, APTT (Activated Partial Thromboplastin Time) was examined by kaolin-cephalin method, PT (Prothrombin Time) was examined by micro rapid method.

## Results

### Effect of brain-cor injection of Ginkgo on serum lipid content in experimental model of hyperlipemia

**Effect of brain-cor injection of Ginkgo on serum TC content in experimental model of hyperlipemia:** As shown in Table 1, TC content was 126.8 $\pm$ 6.2 mg/dl, 137.1 $\pm$ 6.6 mg/dl in study group No 2 and No 1 respectively, and TC content of study groups decreased in contrast with control group (168.5 $\pm$ 8.8 mg/dl) significantly (respectively P<0.01, P<0.05). There was no difference of TC content between study group No 1 and No 2, but TC content of study group No 2 decreased more in contrast with study group No 1.

**Effect of brain-cor injection of Ginkgo on serum TG content in experimental model of hyperlipemia:** As shown in Table 2, TG content was 163.5 $\pm$ 11.9 mg/dl, 178.4 $\pm$ 12.7 mg/dl in study group No 2 and No 1 respectively, and TG content of study groups decreased in contrast with control group (235.6 $\pm$ 15.6 mg/dl) significantly (respectively P<0.01, P<0.05). There was no difference of TG content between study group No 1 and No 2, but TG content of study group No 2 decreased more in contrast with study group No 1.

**Effect of brain-cor injection of Ginkgo on serum HDL-C content in experimental model of hyperlipemia:** As shown in Table 3, HDL-C content was 36.5 $\pm$ 1.6 mg/dl, 33.1 $\pm$ 1.3 mg/dl in study group No 2 and No 1 respectively, and HDL-C content of study groups increased in contrast with control group (27.2 $\pm$ 1.4 mg/dl) significantly (P <0.01). There was no difference of HDL-C content between study group No 1 and No 2, but HDL-C content of study group No 2 increased more in contrast with study group No 1.

### Effect of brain-cor injection of Ginkgo on blood coagulability in experimental model of thrombosis

**Effect of brain-cor injection of Ginkgo on BT and CT in experimental model of thrombosis:** As shown in Table 4, BT was 77.0 $\pm$ 5.9 seconds, 72.0 $\pm$ 5.1 seconds in study group No 2 and No 1 respectively, and BT of study groups was prolonged in contrast with control group (58.0 $\pm$ 4.2 seconds) significantly (P<0.05). There was no difference of BT between study group No 1 and No 2, but BT of study group No 2 was prolonged more in contrast with study group No 1.

**Table 1:** Effect of brain-cor injection of Ginkgo on serum TC content in experimental model of hyperlipemia ( $\bar{x}\pm$ SE).

Groups	Drugs	Dose (mg/kg)	Number of rats (heads)	TC (mg/dl)
Normal group	-	-	10	111.4 $\pm$ 5.3
Control group	-	-	10	168.5 $\pm$ 8.8
Study group No 1	Cor injection of Ginkgo	10	10	137.1 $\pm$ 6.6 <sup>*</sup>
Study group No 2	Brain-cor injection of Ginkgo	10	10	126.8 $\pm$ 6.2 <sup>**</sup>

<sup>\*</sup>p<0.05; <sup>\*\*</sup>p<0.01(comparison with control group).

**Table 2:** Effect of brain-cor injection of Ginkgo on serum TG content in experimental model of hyperlipemia ( $\bar{x}\pm SE$ ).

Groups	Drugs	Dose (mg/kg)	Number of rats (heads)	TG (mg/dl)
Normal group	-	-	10	135.8±7.6
Control group	-	-	10	235.6±15.6
Study group No 1	Cor injection of Ginkgo	10	10	178.4±12.7 <sup>*</sup>
Study group No 2	Brain-cor injection of Ginkgo	10	10	163.5±11.9 <sup>**</sup>

<sup>\*</sup>p<0.05; <sup>\*\*</sup>p<0.01(comparison with control group).

**Table 3:** Effect of brain-cor injection of Ginkgo on serum HDL-C content in experimental model of hyperlipemia ( $\bar{x}\pm SE$ ).

Groups	Drugs	Dose (mg/kg)	Number of rats (heads)	HDL-C (mg/dl)
Normal group	-	-	10	41.6±2.1
Control group	-	-	10	27.2±1.4
Study group No 1	Cor injection of Ginkgo	10	10	33.1±1.3 <sup>**</sup>
Study group No 2	Brain-cor injection of Ginkgo	10	10	36.5±1.6 <sup>**</sup>

<sup>\*\*</sup>p<0.01(comparison with control group).

**Table 4:** Effect of brain-cor injection of Ginkgo on BT and CT in experimental model of thrombosis ( $\bar{x}\pm SE$ ).

Groups	Drugs	Dose (mg/kg)	Number of rats (heads)	BT (S)	CT (S)
Normal group	-	-	10	94.7±7.6	237.0±21.8
Control group	-	-	10	58.0±4.2	104.0±11.2
Study group No 1	Cor injection of Ginkgo	10	10	72.0±5.1 <sup>*</sup>	168.0±12.3 <sup>**</sup>
Study group No 2	Brain-cor injection of Ginkgo	10	10	77.0±5.9 <sup>*</sup>	186.0±16.7 <sup>**</sup>

<sup>\*</sup>p<0.05; <sup>\*\*</sup>p<0.01(comparison with control group).

**Table 5:** Effect of brain-cor injection of Ginkgo on APTT and PT in experimental model of thrombosis ( $\bar{x}\pm SE$ ).

Groups	Drugs	Dose (mg/kg)	Number of rats (heads)	APTT (S)	PT (S)
Normal group	-	-	10	33.3±1.9	23.6±2.6
Control group	-	-	10	18.7±1.5	13.3±1.4
Study group No 1	Cor injection of Ginkgo	10	10	25.2±1.7 <sup>*</sup>	18.8±1.8 <sup>*</sup>
Study group No 2	Brain-cor injection of Ginkgo	10	10	28.5±1.6 <sup>**</sup>	21.2±2.1 <sup>**</sup>

<sup>\*</sup>p<0.05; <sup>\*\*</sup>p<0.01(comparison with control group).

And CT was 186.0±16.7 seconds, 168.0±12.3 seconds in study group No 2 and No 1 respectively, and CT of study groups was prolonged in contrast with control group (104.0±11.2seconds) significantly (P<0.01). There was no difference of CT between study group No 1 and No 2, but CT of study group No 2 was prolonged more in contrast with study group No 1.

**Effect of brain-cor injection of Ginkgo on APTT and PT in experimental model of thrombosis:** As shown in Table 5, APTT was 28.5±1.6 seconds, 25.2±1.7 seconds in study group No 2 and No 1 respectively, and BT of study groups was prolonged in contrast with control group (18.71.5 seconds) significantly (respectively P<0.01, P<0.05). There was no difference of APTT between study group No 1 and No 2, but APTT of study group No 2 was prolonged more in contrast with study group No 1.

And PT was 21.2±2.1 seconds, 18.8±1.8 seconds in study group No 2 and No 1 respectively, and PT of study groups were prolonged in contrast with control group (13.3±1.4 seconds) significantly (respectively P<0.01, P<0.05). There was no difference of PT between study group No 1 and No 2, but PT of study group No 2 was prolonged more in contrast with study group No 1.

## Discussion

Ginkgo leaves are rich in natural resources and its therapeutic

effects are well-advertised. Up to now numerous studies for the treatment of disease with ginkgo leaves were progressed and in the process of study medicines and health food such as Ginkgo pills for arteriosclerosis, cor injection of Ginkgo, cor tincture of Ginkgo and Ginkgo tea are standardized and used. But these medicines and health food were prepared from Ginkgo extract with only flavonoid content above 24% without lactone components. Therefore these do not display enough therapeutic value.

Worldwide standardized and used Ginkgo extract consists of flavonoid content above 24%, total lactone content above 6% and total ginkgolic acid content below 5µg/g [1,2]. This Ginkgo extract is acknowledged as natural medicines that are effective in the treatment of cardiovascular and nervous system diseases such as cerebral apoplexy, angina pectoris, hypertension, hyperlipemia, senile dementia, diabetes mellitus and has few side effects [3,4]. Especially it is known that lactone component in Ginkgo extract is a strong natural inhibitor to platelet-activating factors. At present Ginkgo preparation has become one of the medicines in high demand in the treatment of cardiovascular and nervous system diseases [5,6].

On the other hand female hormone preparation is limited in long term use because of hyperlipemia and thrombosis that are complications occurring in long term use of female hormone preparations for dysfunctional uterine bleeding, climacteric

disorder, female genital organs tumor [7-12]. Therefore to prevent complications such as hyperlipemia and thrombosis with female hormone preparation use are the acute problems not only for the effective treatment of gynecological diseases but also for the lowering of incidence rate of hypertension, arteriosclerosis, hyperlipemia and thrombosis.

We made brain-cor injection of Ginkgo for the treatment hyperlipemia and thrombosis that are complications occurring in long term use of female hormone preparations. Our brain-cor injection of Ginkgo consists of flavonoid content above 24% and total lactone content above 6% and total ginkgolic acid content below 5  $\mu\text{g/g}$ . We verified its effects on serum lipid content in experimental model of hyperlipemia and on blood coagulability in experimental model of thrombosis.

According to our research data, brain-cor injection of Ginkgo decreased serum TC and TG content and increased serum HDL-C content in experimental model of hyperlipemia. On the other hand brain-cor injection of Ginkgo showed more therapeutic effect on hyperlipemia in contrast with cor injection of Ginkgo used previously. And serum TC and TG content, serum HDL-C content with brain-cor injection of Ginkgo did not reach normal value, but it tended to reach the value similar to normal value.

According to our research data, brain-cor injection of Ginkgo prolonged BT, CT, APTT and PT significantly in experimental model of thrombosis. On the other hand brain-cor injection of Ginkgo showed more therapeutic effect on thrombosis in contrast with cor injection of Ginkgo used previously. And some parameters for coagulation with brain-cor injection of Ginkgo did not reach normal value, but it tended to reach the value similar to normal value. We recognized that the results mentioned above depend on brain-cor injection of Ginkgo, because it contains not only flavonoid but also lactone above 6%. And we predict that using Ginkgo extract containing lactone components as medicinal substances is a way for the improvement of therapeutic effects because lactone components have strong antithrombotic and antihyperlipemic action.

Therefore our brain-cor injection of Ginkgo can be used for the treatment of hyperlipemia and thrombosis that are complications occurring in long term use of female hormone preparations for dysfunctional uterine bleeding, climacteric disorder, female genital organs tumor. However the study for clinical application of this medicine must be continued in future.

## Conclusion

Brain-cor injection of Ginkgo decreased serum TC and TG content and increased serum HDL-C content in experimental model of hyperlipemia, and brain-cor injection of Ginkgo decreased blood coagulability in experimental model of thrombosis significantly.

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