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Research Article

THE EFFECT OF "ANTISCHEMIN" PREPARATION ON COAGULATION IN DIABETIC MODEL

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ABSTRACT

In a common case of atherosclerosis and diabetes promote vascular endothelial disease, disorder of brain and heart function among human population, loss of cellular regulation which is tightly involved to circulation of electron and proton in 14 billion cell complex, named "The membrane-redox potentials three-state line system dependent-full 9 stepped cycle of proton conductance" and deficiency of oxygen for energy and metabolism are a main causes for cell mediated every disorders in human body. Therefore, this research study is aimed to introduce new medicine named Antischemin for prevention of cellular disorder in metabolism and improvement of blood circulation and regulation of blood coagulation at the pathogenic models.

Conclusion: In acute, subacute and chronic phase of diabetic model, comparing to INR, PT had no difference but INR had increased by 8.8-14.4%, aPTT increased by 10.26-40.9%, TT increased by 17.3-29.7% and fibrinogen increased by 30-60.5%. This indicates thrombocyte activation and aggregation in blood circulation is more significant on days 3-14. Comparing Antischemin group with 100 mg/kg and control group, there was no difference in PT but INR, aPTT and TT increased by 16.6-18.8%, 10-24.8% and 12.35-33.25% respectively. Fibrinogen decreased by 40.5% indicating that it inhibits thrombocyte aggregation, coagulation and increased blood rheologic properties in blood.

INTRODUCTION

Among the noncommunicable diseases of the world, people are mostly affected by heart disease, stroke, cancer, diabetes and lung disease, and specially in underdeveloped and developing countries. [1] According to UN specialized-agency team report in 2015-2016, 77 percent of total mortality was non-communicable disease [2] and diabetes, stroke were 5 leading causes. The Sustainable Development goal of the United Nations until 2030 is to maintain 25% in arterial hypertension, obesity, and diabetes [3]. In most common disease such as atherosclerosis and diabetes, the main cause of the vascular endothelial damage causing metabolic imbalance in vital organs such as brain and heart is the oxygen deficiency and proton-electron flow loss of "9-step circuits of proton-electron flow in 14 billion cells of human body". [4,5,7] Thus, within pathophysiologic path multi-factor dependent levels, producing blood thinning, blood supply increasing thereby preventing metabolic imbalance medicine is our basis.

Purpose

Study the effects of Astragalus membranaceus, Scutellaria baicalensis, and Gingko bilobabased Antischemin preparation on coagulation.

MATERIALS AND METHODS

The study was conducted by the Center for Innovation of the New Medical Science University, ELISA laboratory, Gyals center and Pretcilab laboratories and selected 30 healthy rabbits weighing 2,3-2,8 kilograms from national biotechnology industry in Mongolia. Rabbits were divided into 4 groups;group 1 or healthy group, group 2 or control group without medication, group 3 or experimental group with Antischemin (1: 1: 1) at 100 mg / kg, and group 4 or comparing group with Clopidegrole with 2.14 mg / kg orally for 5 days respectively and 5 days after a 6% Alloksan monohydrate (Sigma Chemicals, USA) solution was injected through rabbit ear IV with 60 mg / kg by Lukenes (1948); Gaulton et al (1985) method and created diabetes model. developed a pathogenic

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disorder for diabetes. Specific parameters such as prothrombin time (PT-s), INR, fibrinogen (g / l), thrombin time (TT-s), and activated thromboplastin time (aPTT-s) were measured on day 3, 7, 14, 21 and 28.

RESULT

On day 3, comparing control group with healthy group, prothrombin time decreased by 0.28 sec, INR by 11,8% aPTT by 3.8 sec or 17.9% (in healthy group 21.2±2.11, in control group 17.4±1.36, P<0.05), and thrombin time by 5.7sec or 27.6% (in healthy group 20.6±2.15, in control group 14.9±1.69, P<0.05) respectively and fibrinogen increased by 12.9%, indicating increased blood viscosity.

Table 1 The effect of Antischemin on coagulogram on day 3 in diabetic rabbit model with Allokson.

Group	Parameters				
	PT (sec)	INR	APTT(sec)	Fibrinogen (g/l)	TT (sec)
Healthy (n=6)	8.95±0.96	0.93±0.021	21.2±2.11	2.7±0.16	20.6±2.15
Control (n=6)	8.67±1.06	0.82±0.045*	17.4±1.36	3.1±0.22*	14.9±1.69*
Antischemin (n=6)	8.75±0.34	0.88±0.041	19.1±1.46	2.13±0.14**	17±2.36*
Clopidogrel (n=6)	9.9±0.96**	0.93±0.014**	19.4±1.78	1.93±0.07**	16±1.89

*- When control group is compared to healthy group P≤ 0.05, P≤ 0.001
**- When treated group is compared to control group P≤ 0.05, P≤ 0.001

On day 3 of experimental group with Antischemin by 100mg/kg, PT and INR did not have significant difference comparing to control group but fibrinogen was decreased by 31.29% (Antischemin group 2.13±0.14, control group 3.1±0.22, P<0.05), aPTT and TT were shortened by 9.9% or 1.7 sec an 12.35% respectively (Antischemin group 17±2.36, control group 14.9±1.69, P<0.05).

Table 2 The effect of Antischemin on coagulogram on day 7 in diabetic rabbit model with Allokson.

Group	Parameters				
	PT (sec)	INR	APTT(sec)	Fibrinogen (g/l)	TT (sec)
Healthy (n=6)	10.4±1.36	0.90±0.03	25.6±2.03	1.5±0.07	19.0±2.36
Control (n=6)	9.6±2.06	0.82±0.02	17.8±2.36*	3.8±0.09*	13.35±1.25*
Antischemin (n=6)	10.83±2.65**	1.01±0.014**	23.7±1.45**	2.26±0.04**	20±1.36**
Clopidogrel (n=6)	10.2±2.04	0.95±0.07	20.75±2.47**	2.75±0.1**	21.0±3.02**

*- When control group is compared to healthy group P≤ 0.05, P≤ 0.001
**- When treated group is compared to control group P≤ 0.05, P≤ 0.001

On day 7 of the trial, comparing control group with healthy group, prothrombin time decreased by 0.8 sec, INR by 8,8%, aPTT by 7.8 sec or 30.4% (in healthy group 25.6±2.03, in control group 17.8±2.36, P<0.001), and thrombin time by 5.65sec or 29.7% (in healthy group 19.0±2.36, in control group 13.35±1.25, P<0.001) respectively and fibrinogen increased by 60.5% (in healthy group 1.5±0.07, in control group 3.8±0.09, P<0.001), indicating increased blood viscosity more comparing to day 3 result.

But in group with Antischemin by 100mg/kg, PT decrease by1.23 sec or 11.35% (Antischemin group 9.6±2.06, control group 10.83±2.65, P<0.05), INR by 18.8%, (Antischemin group 0.82±0.02, control group 1.01±0.014, P<0.05), aPTT by 5.9sec or 24.8% (Antischemin group 23.7±1.45, control group 17.8±2.36, P<0.05), and TT by 6.65 sec or 33.25% (Antischemin group 20±1.36, control group 13.35±1.25, P<0.05), shortened respectively, fibrinogen was decreased by 40.5% (Antischemin group 2.26±0.04, control group 3.8±0.09, P<0.05).

Table 3 The effect of Antischemin on coagulogram on day 14 in diabetic rabbit model with Allokson.

Group	Parameters				
	PT (sec)	INR	APTT(sec)	Fibrinogen (g/l)	TT (sec)
Healthy (n=6)	9.3±1.06	0.87±0.03	28.8±2.03	0.7±0.04	20.7±1.9
Control (n=6)	8.3±2.03	0.81±0.04	17±2.01*	2.6±0.06*	15.6±2.6*
Antischemin (n=6)	9.4±1.89**	0.87±0.07	20.1±2.36**	2.13±0.03**	18.5±1.36**
Clopidogrel (n=6)	10.5±2.04**	0.98±0.06**	19.1±2.36**	2.1±0.07**	16.9±1.36

*- When control group is compared to healthy group P≤ 0.05, P≤ 0.001
**- When treated group is compared to control group P≤ 0.05, P≤ 0.001

On day 14 of the trial, comparing control group with healthy group, prothrombin time decreased by 1.0 sec, INR by 6.89%, aPTT by 11.8 sec or 40.9% (in healthy group 28.8±2.03, in control group 17±2.01, P<0.001), and thrombin time by 5.1sec or 24.6% (in healthy group 20.7±1.9, in control group 15.6±2.6, P<0.05) respectively and fibrinogen increased by 73% (in healthy group 0.7±0.04, in control group 2.6±0.06, P<0.001), indicating blood viscosity even more comparing to day 3 and day 7 result.

But in group with Antischemin by 100mg/kg, PT decrease by 1.1 sec or 11.7% (Antischemin group 8.3±2.03, control group 9.4±1.89, P<0.05), INR by 6.89%, aPTT by 3.1sec or 15.42% (Antischemin group 20.1±2.36, control group 17±2.01, P<0.05), and TT by 2.9 sec or 15.6% (Antischemin group 18.5±1.36, control group 15.6±2.6, P<0.05), shortened respectively, fibrinogen was decreased by 18% (Antischemin group 2.26±0.04, control group 3.8±0.09, P<0.05)meaning flavonoid and phenol in preparation ingredient have decreasing effect on coagulation.

In comparing group with Clopidogrel by 1mg/kg, PT increase by 2.2 sec or 21% (control group 8.3±2.03, Clopidogrel group 10.5±2,04), INR by 17.3% (control group 0.81±0,04, Clopidogrel group 0.98±0,06), aPTT by 2.1sec or 14.2% (control group 17±2,01, Clopidogrel group 19.1±2,36, P<0.05), and TT by 1.3 sec or 7.69% lengthened respectively, fibrinogen was decreasedby 20% (control group 2.6±0,06, Clopidogrel group 2.1±0,07, P<0.05) meaning Antischemin and Clopidogrel has same blood thinning activation.

Table 4 The effect of Antischemin on coagulogram on day 21 in diabetic rabbit model with Allokson.

Group	Parameters				
	PT (sec)	INR	APTT(sec)	Fibrinogen (g/l)	TT (sec)
Healthy (n=6)	8.2±1.06	0.77±0.03	19±2.03	2.1±0.04	20.8±1.9
Control (n=6)	8.1±0.42	0.70±0.04	17.05±0.21	3.0±0.06*	16.35±2.6*
Antischemin (n=6)	9.03±0.21**	0.84±0.02**	19.2±0.15**	2.53±0.32**	20.8±2.15**
Clopidogrel (n=6)	8.7±0.56	0.82±0.05**	19.95±0.49**	1.795±0.29**	19.3±0.98**

*- When control group is compared to healthy group P≤ 0.05, P≤ 0.001
**- When treated group is compared to control group P≤ 0.05, P≤ 0.001

On day 14 of the trial, comparing control group with healthy group, prothrombin time have not changed, INR decreased by 9.09% (in healthy group 0.77±0.03, control group 0.70 ±0.04), aPTT by 1.59 sec or 10.26% (in healthy group 19±2.03, in control group 17.05±0.21), and thrombin time by 21.4% (in healthy group 20.8±1.9, in control group 16.35±2.6, P<0.001)

shortened respectively and fibrinogen increased by 30% (in healthy group 2.1±0.04, in control group 3±0.06, P<0.001), indicating even though blood coagulation dysfynction occursin chronic phase of diabetes, the result is relatively weak comparing to day 3, 7 and 14.

Comparing group with Antischemin to healthy group, PT increase by 0.93 sec or 10.3% (Antischemin group 8.1±0.42, control group 9.03±0.21, P<0.05), INR by 16.6% (Antischemin group 0.84±0.02, control group 0.70±0.04, P<0.05),, aPTT by 2.15 sec or 11.2% (Antischemin group 19.2±0.15, control group 17.05±0.21, P<0.05), and TT by 4.45 sec or 21.4% (Antischemin group 20.8±2.15, control group 16.35±2.6, P<0.001), shortened respectively, fibrinogen was decreased by 15.6% (Antischemin group 2.26±0.04, control group 3.8±0.09, P<0.05) and having inhibiting effect on coagulation.

In comparing group with Clopidogrel by 1mg/kg, PT has no change, INR increased by 14.6% (control group 0.70±0,04, Clopidogrel group 0.82±0,05), aPTT by 2.9sec or 14.53% (control group 17.05±0,21, Clopidogrel group 19.95±0,49, P<0.001), and TT by 2.95 sec or 15.28% (control group 16.35±2.6, Clopidogrel group 19.3±0,98, P<0.001), lengthened respectively, fibrinogen was decreased by 40.2% (control group 3.0±0,06, Clopidogrel group 1.795±0,98, P<0.001).

Table 5 The effect of Antischemin on coagulogram on day 28 in diabetic rabbit model with Allokson.

Group	Parameters				
	PT (sec)	INR	APTT(sec)	Fibrinogen (g/l)	TT (sec)
Healthy (n=6)	10.4±1.06	0.97±0.03	19±2.03	1.8±0.04	20.8±1.9
Control (n=6)	9.75±0.21	0.83±0.02*	17.05±0.21	2.95±0.35*	17.2±0.78*
Antischemin (n=6)	9.6±0.52	0.90±0.05	19.2±0.15	2.54±0.07**	19.3±0.83
Clopidogrel (n=6)	10.3±0.56	0.96±0.03**	19.95±0.49**	1.75±0.21**	18.2±0.07

*- When control group is compared to healthy group P≤ 0.05, P≤ 0.001
**- When treated group is compared to control group P≤ 0.05, P≤ 0.001

On day 28 of the trial, comparing control group with healthy group, PT and aPTT had no statistical significance but INR decreased by 14.4% (in healthy group 0.97±0.03, control group 0.83 ±0.02) and thrombin time by 17.3% (in healthy group 0.97±0.3, in control group 0.83±0.02, P<0.05) shortened respectively and fibrinogen increased by 39% (in healthy group 1.8±0.04, in control group 2.95±0.35, P<0.001) meaning keeping the increased coagulation status.

During this period, in group with Antischemin comparing to healthy group, INR and PT had no statistical significance. On the other hand, aPTT increased by 11.2% (Antischemin group 19.2±0.15, control group 17.05±0.21), and TT by 10.9% (Antischemin group 19.3±0.83, control group 17.2±0.78), shortened respectively, but still had no statistical significance. Fibrinogen was decreased by 13.9% (Antischemin group 2.54±0.07, control group 2.95±0.35, P<0.05).

In comparing group and control group, PT had no change, INR increased by 13.54% (control group 0.83±0,02, Clopidogrel group 0.96±0,03), aPTT by 14.5% (control group 17.05±0,21, Clopidogrel group 19.95±0,49, P<0.05), and TT by 5.5%lengthened respectively, fibrinogen was decreased by 40.6% (control group 2.95±0,35, Clopidogrel group 1.75±0,21, P<0.001) proving that some parameters are same as Antischemin's.

DISCUSSION

As a result of our study, as coagulagram parameters increase by coagulation dysfunction, platelet gather in inflammatory locals and platelet distribution with in red blood cell, immature platelet size and thrombocyte indexes such as thrombocrit increases and inducing thrombocyte aggregation and cluster, thereby adversely affecting the blood rheology properties and induce the pathogenic line. In contrast to this, in animals that used Antischemin preparation, these factors have been decreased, affecting thrombocytes aggregation, coagulation, and improving blood rheological viscosity in micro-cellular level, which are the effects of flavonoids and phenols compounds contained in them. X.Dang, JJ. Research on Miao's antithrombotic effect of RSNK in blood-stasis model rats, Sheng Nao Kang's traditional Chinese medicine has been investigated for the ischemic re-perfusion injury of the brain, which is contained in the composition of Antischemin, the Astragalus has been shown to eliminate blood stasis and obstruction in the collateral vessels. Study of these three plants on immune system, pain, cellular protection, [8-17] new vascular zone and anti-hypoxic activity have been done and Antischemin had more activity.

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