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Efficacy and Safety Study Report of Novel Herbal Formulation-Delstrok Tablets

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ABSTRACT

Cardiovascular disease are non-communicable that has become a serious health problem worldwide. The aim of the study was to evaluate the safety and efficacy of a novel herbal liquid formulation "DELSTROK® ". The toxicity study was performed to evaluate the oral acute toxicity of DELSTROK® in rats and to identify the Thrombolytic efficacious dose of DELSTROK®. The toxicity study was carried out at different doses and it was concluded that the LD_{50} value for DELSTROK® was more than 2000 mg/kg. The efficacy study was carried out and from this study it was concluded that the thrombolytic effect of DELSTROK® is comparable to the commercially thrombolyte, streptokinase. Thus, in this study the LD_{50} for DELSTROK® was obtained and also DELSTROK® was found to show thrombolytic effect. found to show thrombolytic effect.

Keywords: *Delstrok; Herbal Formulation; Thrombolytic; Oral Toxicity; Cardiovascular Diseases.*

1.0 Introduction

Atherosclerosis is one of the leading causes of death, particularly in developed countries where a higher percentage of atherosclerotic deaths are observed. Inhibition of coagulation and thrombus formation are considered to be good strategies to prevent atherosclerosis and cardiovascular diseases [5]. Thrombus is an abnormal blood clot inside a blood vessel [1]. The degradation of the thrombus is brought about by the fibrinolytic system, activated by tissue-type plasminogen activator (t-PA) which converts zymogen plasminogen to plasmin.

Plasmin specifically degrades fibrin, the main component of thrombus, this process is called fibrinolysis/thrombolysis [2]. Commonly used thrombolytic agents are alteplase, anistreplase, streptokinase, urokinase and tissue plasminogen activator (TPA) to dissolve clots [1]. The main objective of this research work was to develop herbal formulation effective against thrombosis or thrombus.

Unlike allopathic medicines, there is no risk factor in using plant based medicine [3]. Medicinal plants and herbs have various active principles with therapeutic potential and their constituents offer exciting opportunity to develop them into novel formulations [4].

2.0 Materials and Methods

The Herbal formulation DELSTROK ® was prepared and the formulation was assessed for microbial count, heavy metals, pesticide and phytochemicals before subjecting to safety and efficacy studies.

2.1. Study plan and design

2.1.1 The toxicity study was performed to assess the toxicity of DELSTROK® when administered through oral route by gavage as a single dose in rats. The study was conducted with Sprague Dawley rats weighing about 142.67 – 158.31 g.

The animals were acclimatized for a period of 05 days to laboratory conditions and were fed with *ad libitum*. The dose volume was 10 ml/kg body weight for all the animals and total duration of the study was 25 days.

All the animals were observed for changes in body weights, clinical signs, mortality and were subjected to detailed pathological examinations (Table 1).

2.1.2 The study to evaluate the efficacious dose of DELSTROK® for its thrombolytic effect [50] was carried out for 14 days (Table 2).

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The study was carried out with Sprague Dawley rats acclimatized for a period of 05 days to laboratory conditions and were fed with *Ad Libitum*. The animals were administered orally with DELSTROK® for a period of 06 days.

All the animals were observed for their feed consumption, body weight, clinical signs, pathology, hematology and gross necropsy.

3.0 Results and Discussion

The toxicity study of DELSTROK® in Sprague Dawley rats was performed as per OECD guidelines, there were no treatment related changes in body weight and percent body weight gain over the study period at all the doses tested.

Table 1: Study Design

No. of Groups	No. of Animais Dosed at a Time	Test Item	Starting Dose Level (Mg/Kg)	Sigma	Upper Bound Dose (Mg/Kg)	Maximum No. of Animals to Complete Limit Test if Upper Bound is Obtained
1	1#	DELSTROK	300	0.5	2000	5

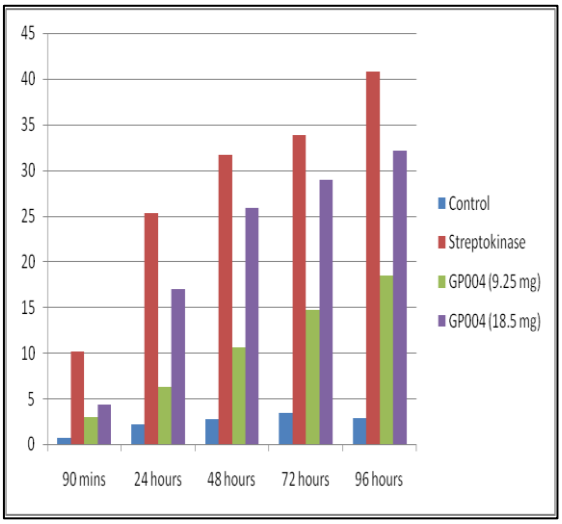
Table 2: The Animals were Divided into Groups as Follows

Tube No.	Vol of Blood (µl)	Incubation	Weight of the clot before lysis(W1)	Conc of test item/100µL	Incubation	Weight of clot after lysis(W2)	% clot lysis = (W2/W1)X100
1-3	500	37±1°C 45 minutes	Weight of the clot before lysis(W1)	Distilled water	37±1°C 90 minutes	Weight of clot after lysis(W2)	% clot lysis = (W2/W1)X100
4-6				Streptokinase			
7-9				9.25 mg			
10-12				18.5 mg			
13-15				Distilled water	37±1°C 24 hours		
16-18				Streptokinase			
19-21				9.25 mg			
22-24				18.5 mg			
25-27				Distilled water	37±1°C 48 hours		
28-30				Streptokinase			
31-33				9.25 mg			
34-36				18.5 mg			
37-39				Distilled water	37±1°C 72 hours		
40-42				Streptokinase			
43-45				9.25 mg			
46-48				18.5 mg			
49-51				Distilled water	37±1°C 96 hours		
52-54				Streptokinase			
55-57				9.25 mg			
58-60				18.5 mg			

There were no clinical signs of toxicity and mortalities observed in the doses tested.

The efficacy study of DELSTROK® for its thrombolytic effect in Sprague Dawley Rats showed a thrombolytic activity at 18.5 mg concentration which is almost similar to the commercially available thrombolyte, Streptokinase (Table 3).

Fig 1: Graphical Representation of Clot Lysis (%) at Different Time Intervals



Cardiovascular disease (CVD) is a term for all diseases of the heart and circulation, including heart disease, stroke, heart failure, cardiomyopathy and atrial fibrillation [8]. Cardiovascular diseases (CVD) are the number one cause of death globally [5], and there is a well-established relationship between low-density lipoprotein and coronary heart disease [9]. The LD_{50} for DELSTROK® in the present study was more than 2000 mg/kg when dosed at different doses for a period of 14 days. Similarly, the LD_{50} for methanolic extract of Tridax procumbens was found to be less than 2000 mg/kg b.w and more than 300 mg/kg b.w. during the 14 day study [9]. Also in another study, the LD_{50} of polyherbal formulation for anti-asthamatic activity was found to be 2262.7 mg/kg, p.o [10].

Thrombolytic agents are used to dissolve the already formed clots in the blood vessels and these drugs sometimes cause serious consequences. Herbal preparations have been used since ancient times for the treatment of several diseases, although they show little toxicity in some cases [11]. In the present study, thrombolytic activity at 18.5 mg concentration after 96 hours incubation was found almost similar to the commercially known thrombolyte, streptokinase. It has been reported that bromelin, a proteolytic enzyme of pineapple, has anti-thrombotic activity *in-vitro*, at concentrations above 10 mg/ml [12]. It has been demonstrated *in-vivo* that the consumption of berries, which belongs to the family of Rosaceae, enhances fibrinolysis in murine models of thrombosis [9]. The anti-thrombotic properties of garlic and onion have been attributed to organo-sulphur compounds [5,8]. Some fruits and vegetables showed antithrombotic activity that may have an important impact on human health and further studies were considered necessary to establish the compounds and mechanisms that account for these effects [10]. Similarly, in the present study the active principles can be considered responsible for the thrombolytic effect of the herbal formulation, DELSTROK®.

5.0 Conclusions

From the present study, it can be concluded that the Delstrok® was nontoxic up to 2000 mg/kg since there were no evident toxicological signs during the study and thus the LD_{50} value can be concluded to be more than 2000 mg/kg body weight when administered as a single dose. Efficacy evaluation of anti-thrombolytic effect of Delstrok® in Sprague Dawley rats showed that the test item at a concentration of 18.5 mg had thrombolytic activity. The available data indicates that thrombolytic efficiency of Delstrok® is comparable to the commercially available thrombolyte, streptokinase.

Acknowledgment

The intellectual property rights of the product, Delstrok® lies with Goan Pharma P. Ltd and the studies were performed at Liveon Biolabs P. Ltd., Tumkur (46 & 47, Water Tank Road, KIADB Industrial Area, Antharasanahalli, Tumkur-572 106, Karnataka, India).

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