

Comparative Acute Oral Toxicity Study of Cartinovex Plus Verses Anti-arthritis Devil's Claw in Mice

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ABSTRACT

Background: Devil's Claw (*Harpagophytum procumbens*) is herb which is suggested for the management of arthritis as a home remedy. Glucosamine is a another naturally occurring aminomonosaccharide present in articular cartilage of joints and synovial fluid. We established an oral tablet with the name of Cartinovex Plus having glucosamine with HA and Methyl sulfonyl methan for the pain of arthritis and compare with dewil's claw for toxicity levels

Aims and objectives: The study was completed to assess the comparison of acute oral toxicity of the CartiNovex extract with Anti-arthritis Devil's Claw extract in the NMRI strain of mice.

Methodology: This study will provide genuine in-house generated information reflecting pre-clinical toxicity of CartiNovex Plus and Anti-arthritis Devil's Claw product, which will increase our confidence in the product and will facilitate the registration process. NMRI mice were obtained from Animal house facility on standard environmental conditions i.e. 25 ± 1 °C, relative humidity (RH) 52 - 61% and 12 h dark / light cycle.

Results: No significance results were obtained on physical and behavior changes.

Discussion and Conclusion: No mortality and morbidity were observed and no variation in weights were identified on either groups. It was concluded that both the drugs are potentially safe for use.

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INTRODUCTION

Rheumatoid arthritis (RA) is an inflammatory disease caused by the obliteration of cartilages, bones and joints [1]. Osteoarthritis considered to be the most common form of arthritis, it prevail after 65 years of age and found 60% in men and 70% women. Main etiology related to the mechanical, inflammatory and metabolic causes

however environmental risk factors include trauma, obesity and type of occupational. Most prescribed Non-steroidal anti-inflammatory drugs (NSAIDs) considered to be very effective in serious and moderate pain with some serious gastrointestinal issues. Other compounds such as chondroitin sulfate and glucosamine sulfate

used as a choice of drug with less side effects [2].

Devil's Claw (*Harpagophytum procumbens*) is herb which is suggested for the management of arthritis as a home remedy. The active component include harpagoside, a monoterpenic glucoside belonging to the iridoid class of compounds[3].It has historically been used as an analgesic, stimulate for gastric enzymes and fever [4]. The major chemical component for the anti-inflammatory activity isharpagoside (COX-2 inhibitor). In 2007, A Meta-analyses established for determine the effectiveness of H. procumbens for arthritis symptoms, analgesia and fever.[5-7].

Glucosamine is a another naturally occurring aminomonosaccharide present in articular cartilage of joints and synovial fluid [8]. Some studies have established that glucosamine have more enhanced pain relief characteristics and helps in mobility as compared to placebo [9-15]. It has proven that more than 30 years that Glucosaminesupplements have strong relief action specifically for osteoarthritis[16]. Three types of supplement available for recover the deficiency N-acetyl-glucosamine, glucosamine sulfate and glucosamine hydrochloride [17]. As per Setnikar et al. it metabolized by first pass effect and absorb about 90%[18]. Pharmacokinetics study reveals that human[19] has the same bioavailability as rats[20]. However hyaluronic acid (HA) also play an active role in protecting articular tissues from oxidative damage [21].For bone matrix Chondroitin sulphate (CS) is good for maintaining ligaments and tendons cartilage, skin and blood vessels[22].It was proven in different meta-analysis that the combination of CS and Glucosamine is effective for the treatment of arthritis and considered to be the safe choice[23].

We established an oral tablet with the name of Cartinovex Plus havingglucosamine with HA and

Methyl sulfonyl methan for the pain of arthritis and compare with dewil's claw for toxicity levels.

METHODOLOGY

NMRI mice were selected from in house facility of Herbion Pak. Pvt. Ltd. Animals were kept under standard maintain condition i.e. 25 ± 1 °C, RH 52 - 61% and 12 hour dark / light cycle. As per desired water and feed were provided.Selected animals age were 6-8 weeks at the start of the experiment.After the initial stabilization period average body weight were taken and the range were between 25 – 35 g. All experimental animals were identified properly on cages by cage card number. After initial weights measurements, random distribution of animals were established for the study. Al the procedure of the experimental study were under the premises of the conventional animal house facility of Herbion Pak. Pvt. Ltd.

For acute oral toxicity, Animals were divided into 3 groups i.e. control, Cartinovex and Devil's Claw group with n=10. It was performed on the classic method as per OECD guidelines [24].Mice were treated orally using gastric gavage with doses (1 or 5g/kg) of test product and observe for 7 days. The parameters which were noted were physical and behavioral examination, Mortality & Morbidity, Food Intake and Body Weight Changes.

RESULTS

On physical examination, the test product did not cause any sign of ill health or overalltoxicity atcalculated doses of 1 or 5 g/kg. No hair loss, color loss, heart rate (chest expansion and retraction), writhing, stretching fecal abnormality and respiration was observed in all 3 groups. However no abnormal result seen on Behavioral Examination (table 2).

Table 1: Physical examination of mice with all experimental groups

Drugs	Physical Examination						
	Hair Loss	Color Loss	Heart Rate	Writhing	Stretching	Fecal Abnormality	Respiration
Cartinovex Plus (Aqueous Extract)	N	N	N	N	N	N	N
Devil's Claw (Aqueous Extract)	N	N	N	N	N	N	N
Control (Water)	N	N	N	N	N	N	N

Table 2: Behavioral examination of all experimental animals

Drugs	Behavioral Examination										
	Alertness	Grooming	Restlessness	Touch Response	Aggression	Pain Response	Convulsions	Tremors	Lacrimation	Salivation	Corneal Reflex
Cartinovex Plus (Aqueous Extract)	N	N	N	N	N	N	N	N	N	N	N
Devil's Claw (Aqueous Extract)	N	N	N	N	N	N	N	N	N	N	N
Control (Water)	N	N	N	N	N	N	N	N	N	N	N

N=Normal

No remarkable change in the behavior was noted. All the treated animals retain normal

locomotive and socialization activities. No mortality was observed with doses of 1 and 5 g/kg of all groups (Table.3).

Table 3: Evaluation of mortality on all groups

S.NO	N(Male)	Test Substance	Dose Level (mg/kg)	Mortality (%)
1	10	Cartinovex Plus (Aqueous Extract)	1000	0
			5000	0
2	10	Devil's Claw (Aqueous Extract)	1000	0
			5000	0
3	10	Control (Water)	1000	0
			5000	0

No significant difference between food intake of treated and control groups was noted. Body weights of each animal recorded prior to the test item application day 0, on day 7 and day 14.

No significant differences in the weight were observed between groups exposed to CartiNovex plus, Devil's claw and those receiving the water (control) Table.4.

Table 4: Body weight changes in all different animal groups after testing drugs

Drugs	Species	Dose (mg/kg)	Animals (N)	Body Weight (Day=0) Mean±S.D	Body Weight (Day=7) Mean±S.D	Body Weight (Day14) Mean±S.D
Cartinovex Plus	Mice: NMRI strain	1000	10	29.6±0.702	29.2±0.727	29±0.760
		5000	10	28.8±0.997	28.4±1.146	28.1±1.129
Devil's Claw	Mice: NMRI strain	1000	10	27.2±0.611	27±0.745	27.2±0.757
		5000	10	27±0.954	26.6±1.156	26.8±1.271
Control (Water)	Mice: NMRI strain	1000	10	29.6±0.426	30.4±0.426	30.6±0.520
		5000	10	29.6±0.520	29.4±0.4	29±0.494

CONCLUSION

Oral Cartinovex plus extract is potentially safe as compare to the other experimental groups and does not cause apparent morbidity in the animals. Substantial evidence prove that both H. procumbens and Glucosamine have strong anti-inflammatory effect and well tolerated treatment option for arthritis. They can also be recommended with first line therapy as an adjuvant. It has also proven that the drug contains Glucosamine can improve long term quality of life by minimizing side effects as compare to the anti-inflammatory drugs[25]. Glucosamine with often combination with

chondroitin Sulphate help cartilage matrix for binding and help to relief moderate to severe pain[26]. Present study evidently shows that there was no significantly increase and decrease the weights of male mice as compare to control animals.

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