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Research Article

A Study of Anti-Inflammatory Activity of one Novel C-21 Steroidal Glycoside known as Carumbelloside-IV isolated from *Caralluma umbellata*

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Abstract

The phytochemical study using *Caralluma umbellate* (Asclepiadaceae) whole plant allowed the isolation of a novel C-21 steroidal glycoside, named as carumbelloside–IV. Carumbelloside –IV was evaluated in wistar rats using carraeenan induced left hind paw edema model. The isolated compound was administered in a dose dependant manner. This showed significant anti-inflammatory activity.

Keywords: *Caralluma umbellate*, Asclepiadaceae, steroidal glycoside, anti-inflammatory activity, Carumbelloside-IV

Introduction

Prolonged uses of both steroidal and non-steroidal anti-inflammatory drugs are well known to be associated with peptic ulcer formation Hence, search for new anti-inflammatory agents that retain therapeutic efficacy and yet are devoid of these adverse effects is justified. There is much hope of finding active anti-rheumatic compounds from indigenous plants as these are still used in therapeutics despite the progress in conventional chemistry and pharmacology in producing effective drugs Herbal drugs are being proved as effective as synthetic drugs with lesser side effects.[1-2] As pregnanes and pregnane glycosides are drawing much attention in recent years because of their antitumor and anticancer activities we continued with our studies on pregnane constituents of Caralluma species. *Caralluma umbellate* Haw (Syn: W&A, *Stapelia umbellata* Roxb, *Carulluma campanulata* N.E.Br) belongs to the family Asclepiadaceae, grows wild in dry and arid regions of Chittoor District and several District of Andhra Pradesh, in India is used in flok medicine.[3-4] The tribal people of Chittoor District used stem juice warmed and mixed with turmeric powder for stomach disorder and abdominal pains.[5] From this plant five novel pregnane glycosides viz., Carumbelloside-I, Carumbelloside-II, Carumbelloside-III, Carumbelloside-IV and Carumbelloside-V and a known flavones glycoside, i.e., luteolin-4'-O-neohesperidoside.This flavones glycoside posses potent anti-inflammatory activity.[6,7] To the best of our knowledge, no pharmacological work carried out on carumbelloside-IV, one of the major phytochemical constituent other than Carumbelloside-I.[8-11]

Material and Methods

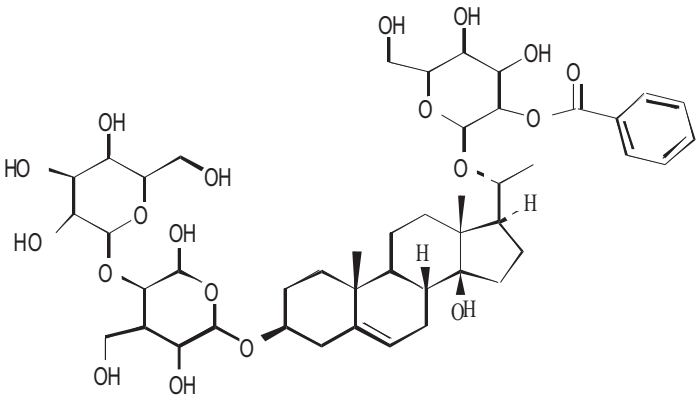
Collection of plant material

Fresh whole plants of *Caralluma umbellata* (Asclepiadaceae), is the thick, erect, leafless, branching, succulent perennial herb collected from Tirumala hills forests of Tirupati in Chittoor district, A.P, India. The herbarium specimen is available in the Department of Botany, Osmania University, Hyderabad, Andhra Pradesh.

Extraction & isolation

The whole fresh plant (9.0kg) was collected and dried for 28 days and then dried plant material are chopped and crushed and passed through sieves (No-60), to made fine free flowing powder. The powder was extracted with EtOH in soxhlet extractor for 9 days at room temperature. The extract was filtered and concentrated under reduced pressure to afford a dark greenish brown semi solid. To concentrate, 2 liter of water was added and extracted successively with toluene, ether, EtOAC and n-BuOH. After evaporation of solvent, the EtOAC extract and n-BuOH extract were subjected to flash silica gel to yield compound A, known as carumbelloside–IV. The n-BuOH extract (48gm) was dissolved in methanol and then chloroform was added until carumbelloside-I precipitated out. It was removed by filtration and filtrate was subjected to silica gel chromatography (10-40µ, 750g) using EtOAC-MeOH-H2O (80:10:10) as the eluent and fraction of 50ml each were collected. Fraction 48-54 contained carumbelloside-IV. Upon TLC examination (Solvent system EtOAC-MeOH-H2O), showed the presence major spots of our interest and was therefore subjected to re chromatography using same system to

purify the compound. The structure of the compound elucidated and identified by extensive spectroscopic methods and molecular modeling.[11-12]



Compound-A: Carumbelloside- IV

Anti-inflammatory activity study of Carumbelloside-IV

The anti-inflammatory activity of the test compounds was evaluated in Wistar rats employing the method of Winter et al.[13-15] Male Wistar rats were used for the study. Animals were fasted overnight and were divided into control, standard and test groups, each containing 6 animals. The test compounds were administered to the animals in the test group at the dose of 10mg/kg, 20mg/kg and 40mg/kg by oral route. Animals in the standard group received Indomethacin at dose of 10mg/kg by oral route. All test and standard compounds were administered as 1% gum acacia suspension. Rats in control group received the vehicle solution without drugs. One hour after drugs administration, rats in all groups were challenged with 0.1 ml of 1% Carrageenan in sub plantar region of left hind paw. A zero hour paw volume was measured for the rats using digital Plethysmo meter (Ugo Basile, Italy Model 7150) before the administration of Carrageenan for all groups. Paw volumes were again measured at 30 min interval for 3h.The mean paw oedema value for test group being compared with its mean value for control group.

Statistical analysis:

All results were expressed as ± S.E.M. The differences between experimental groups were compared by one way ANOVA (Control vs. treatment, Bonferrioni's method) (Using Jindal Scientific Sigmastat Statistical software, Version1.0) and were considered statistically significant when $p < 0.005$

Results and Discussion

In pharmacological studies, Carrageenan-induced rat paw oedema is used in the search for the new anti-inflammatory drug and compared with that of a model anti-inflammatory drug indomethacin utilizing edema model.

The anti-inflammatory activity of Carumbelloside-IV of *Caralluma umbellata* Haw. (Asclepiadaceae) was evaluated by Carrageenan induced rat paw edema method and the result is shown in Table 1. The isolated compound was tested at three different doses level 10mg/kg, 20mg/kg and 40mg/kg in a dose dependant manner. As shown in Table 1, the Carumbelloside-IV, showed maximum inhibitions, 60.4% at the dose of 40mg/kg after 3h of drug treatment in Carrageenan induced paw edema, where as standard drug showed 69.7% of inhibition. The compound up to a dose of 80mg/kg did not produce any toxicity symptoms. The major constituents of the *Caralluma umbellata* have no significant anti-inflammatory activity but have the potent antinociceptive activity. From current study of the isolated compound Carumbelloside- IV of *Caralluma umbellata* showed the significant anti-inflammatory activity on Carrageenan induced rat paw edema method.

Table1: Effect of Carumbelloside-IV on Carrageenan induced paw

Treatment	Dose (mg/kg)	Change in Paw edema mean	%of inhibition
Control	0	0.716±0.070	-----
Indomethacin	10	0.340±0.030	69.7
Carumbelloside-IV	10	0.482±0.040	41.8
Carumbelloside-IV	20	0.435±0.030	52.3
Carumbelloside-IV	40	0.360±0.030	60.4

Note: values are mean S.E.M (n=6). Experimental groups were compared with control $p < 0.005$

Conclusion

In view of our interest in the chemical constituents of indigenous medicinal plants, the chemical examination of the dried whole plant of *Caralluma umbellata* has now been undertaken. The present pharmacological study was undertaken to evaluate the possible anti-inflammatory properties of the isolated C-21 steroidal glycoside named Carumbelloside-IV from the aqueous alcoholic extract from *Caralluma umbellata*. The result of current study confirmed the traditional use of *Caralluma umbellate* for the treatment of painful inflammatory diseases.[16-18]

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