

PHARMACOLOGICAL EVALUATION OF MELOXICAM IMPURITY FOR ANALGESIC AND ANTIINFLAMMATORY ACTIVITIES USING ANIMAL MODELS

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Article Received on 19/10/2022

Article Revised on 09/11/2022

Article Accepted on 29/11/2022

ABSTRACT

Many phenolic compounds have been shown to have anti-inflammatory and analgesic effects. Flavonoids and tannins, which have been detected in phytochemical studies of natural compound ethanolic extricates, may inhibit the production of prostaglandins and bradykinins. We will use the stomach-narrowing effect of acidic corrosion to identify antinociceptive experts who function on the periphery of our nervous system. Experimenters may have discovered that extracts may reduce the number of writhes that animals experience in response to the adverse effects of the boosts. When administered to rats with carrageenan-induced paws, the chemically prepared natural substances significantly reduced inflammation.

KEYWORDS: phenolic compounds, inflammation, natural substances.

INTRODUCTION

Analgesics

A drug that selectively relieves pain by acting in the CNS or on peripheral pain mechanisms, without significantly altering consciousness. A wide range of drugs are used to control pain. They range from mild over-the-counter (OTC) drugs, such as aspirin and acetaminophen, to strong general anaesthetics. Drugs that relieve pain often reduce fever and inflammation that are used to treat conditions such as

- Mild to moderate pain caused by injury or surgery
- Fever, headaches, and painful menstruation
- Rheumatoid arthritis (a chronic inflammatory disease of the peripheral joints)
- Osteoarthritis (a chronic disease that involves wear and deterioration of joints in the body, causing inflammation)
- Chronic pain associated with cancer, AIDS, multiple sclerosis, or sickle cell disease

INFLAMMATION

Inflammation or phlogosis is pathological response of living tissue to injuries that leads to the local accumulation of plasmatic fluid and blood cell. Although it is defense can be induced, maintain or aggravate many disease. It is a complex phenomenon, comprising of biochemical as well as immunological factors. Inflammation is recognized by following symptoms:

1. Rubor (redness)
2. Tumor (Swelling)

3. Calor (heat)
4. Dolor (pain)
5. Functio laesa (Loss of functions)

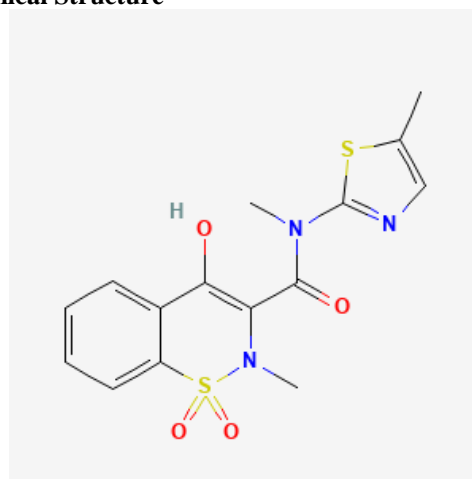
Compound

Amido Methyl Meloxicam (Meloxicam Impurity)

Molecular Formula C₁₅H₁₅N₃O₄S₂

Molecular Weight 365.4

Chemical Structure



IUPAC Name

4-hydroxy-N,2-dimethyl-N-(5-methyl-1,3-thiazol-2-yl)-1,1-dioxo-1λ6,2-benzothiazine-3-carboxamide.

the extract and Diclofenac sodium treated groups was compared with those of animals in the control group⁽⁴⁴⁾.

ANTI-INFLAMMATORY ACTIVITY CARRAGEENAN-INDUCED PAW EDEMA IN RATS

Acute inflammation was produced by injecting 0.1 ml of 1% (w/v) carrageenan suspension into the sub planter region of the right hind paw of the rats. The animals were pre treated with the drug 1hour before the administration of carrageenan⁽⁵¹⁾. The paw thickness was measured at 1, 2, 3 and 4 h after carrageenan injection by using digital vernier callipers.

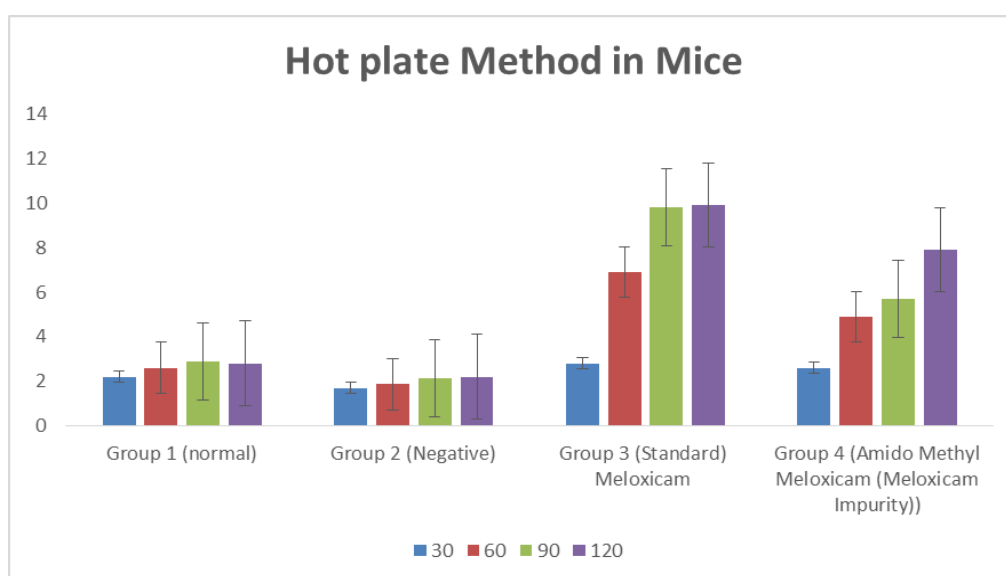
COTTON PELLET INDUCED GRANULOMA METHOD IN RATS

Cotton pellets, weighing 5mg each were sterilized. Under ether anaesthesia, the pellets were introduced subcutaneously through a skin incision on the back of the animals. Starting from 30 min after the implantation of cotton pellet for all the rats.

RESULTS

Hot plate Method in Mice

Treatments	30	60	90	120
Group 1 (normal)	2.2 ± 0.29	2.6 ± 0.43	2.9 ± 0.11	2.8 ± 0.09
Group 2 (Negative)	1.7 ± 0.12	1.868 ± 0.27	2.14 ± 0.10	2.21 ± 0.14
Group 3 (Standard) Meloxicam	2.8 ± 0.18	6.9 ± 0.16	9.8 ± 0.09	9.9 ± 0.13
Group 4 (Amido Methyl Meloxicam (Meloxicam Impurity))	2.6 ± 0.23	4.9 ± 0.18	5.7 ± 0.04	7.9 ± 0.17



Tail Immersion Method

Treatments	0	30	60	90	120
Group 1 (normal)	1.504 ± 0.34	1.402 ± 0.26	1.701 ± 0.28	1.803 ± 0.13	1.904 ± 0.31
Group 2 (Negative)	1.304 ± 0.36	1.705 ± 0.24	1.868 ± 0.25	1.924 ± 0.15	2.156 ± 0.24
Group 3 (Standard) Meloxicam	1.806 ± 0.37	2.604 ± 0.21	4.202 ± 0.19	5.806 ± 0.16	5.402 ± 0.22
Group 4 (Amido Methyl Meloxicam (Meloxicam Impurity))	1.583 ± 0.46	1.684 ± 0.29	1.746 ± 0.26	1.835 ± 0.26	1.932 ± 0.26

The test drugs were administered daily for 7days. On the 8th day, the animals were sacrificed with diethyl ether. The granulomas were removed and the weighed.

EXPERIMENTAL DESIGN

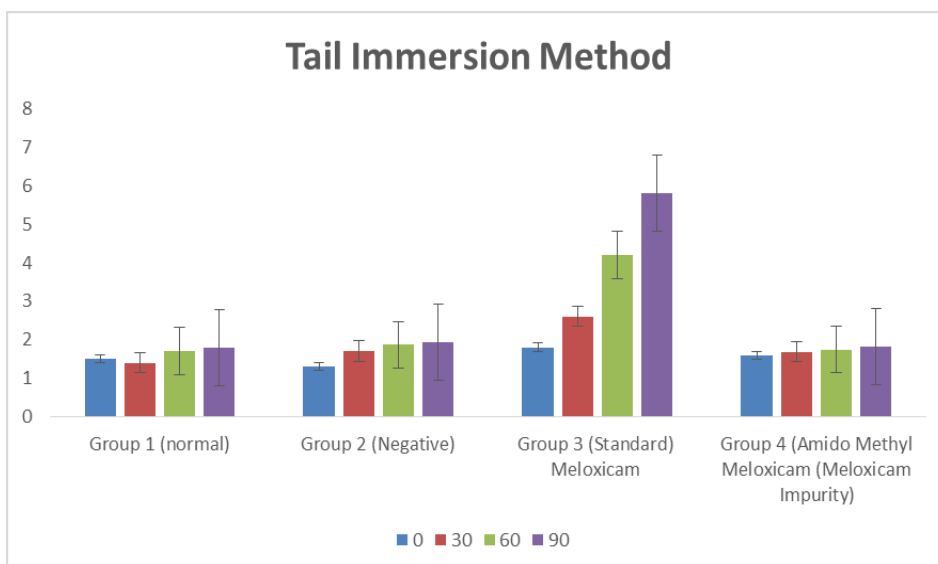
24 rats are divided into 4 groups of six rats each (n=06) and treated orally as follows –

Group-1: (normal): it was used as a normal saline rats seven days.

Group-2: (CMC): rats received distilled water orally daily for seven days,

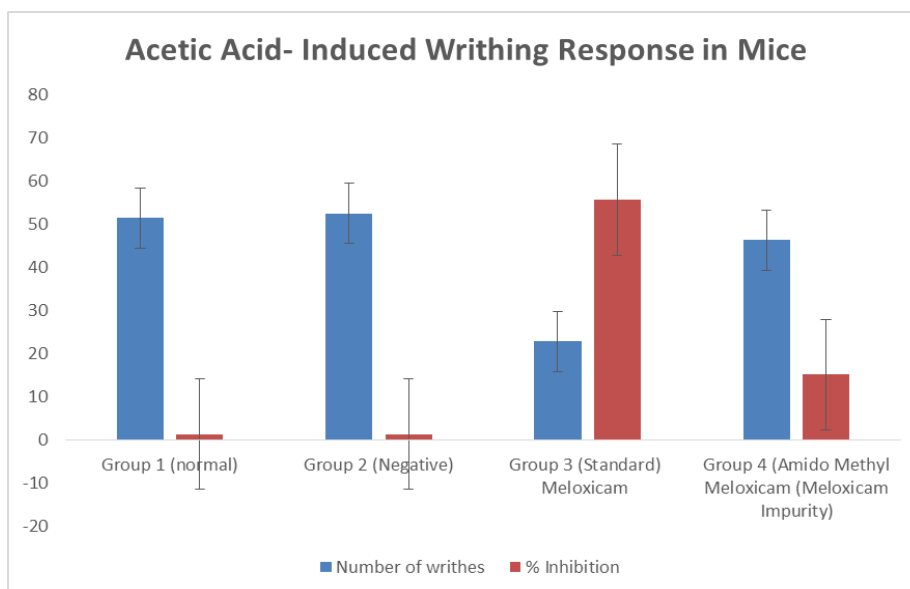
Group – 3: (CMC + MELOXICAM): rats received MELOXICAM orally daily for seven days

Group -4: (CMC + Amido Methyl Meloxicam (Meloxicam Impurity)): rats received extract orally for seven days.



Acetic Acid- Induced Writhing Response in Mice

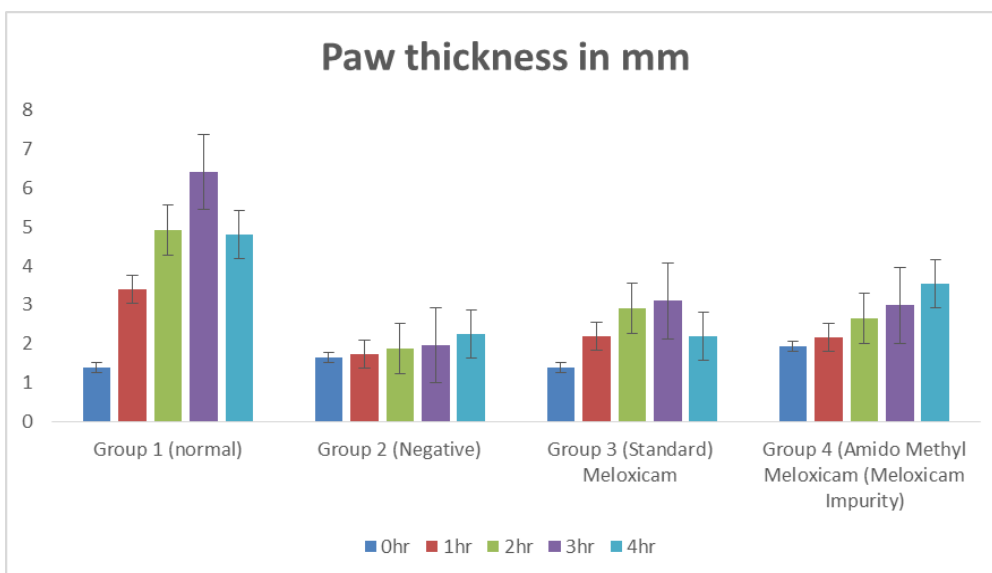
Treatments	Number of writhes	% Inhibition
Group 1 (normal)	51.464 ± 0.33	1.402 ± 0.33
Group 2 (Negative)	52.478 ± 0.26	1.412 ± 0.34
Group 3 (Standard) Meloxicam	22.819 ± 0.21	55.64 ± 0.28
Group 4 (Amido Methyl Meloxicam (Meloxicam Impurity))	46.358 ± 0.36	15.17 ± 0.22



Carrageenan-Induced Paw Edema in Rats

Anti inflammatory activity of ethanolic extract of Organic compounds on Carrageenan induced paw edema method.

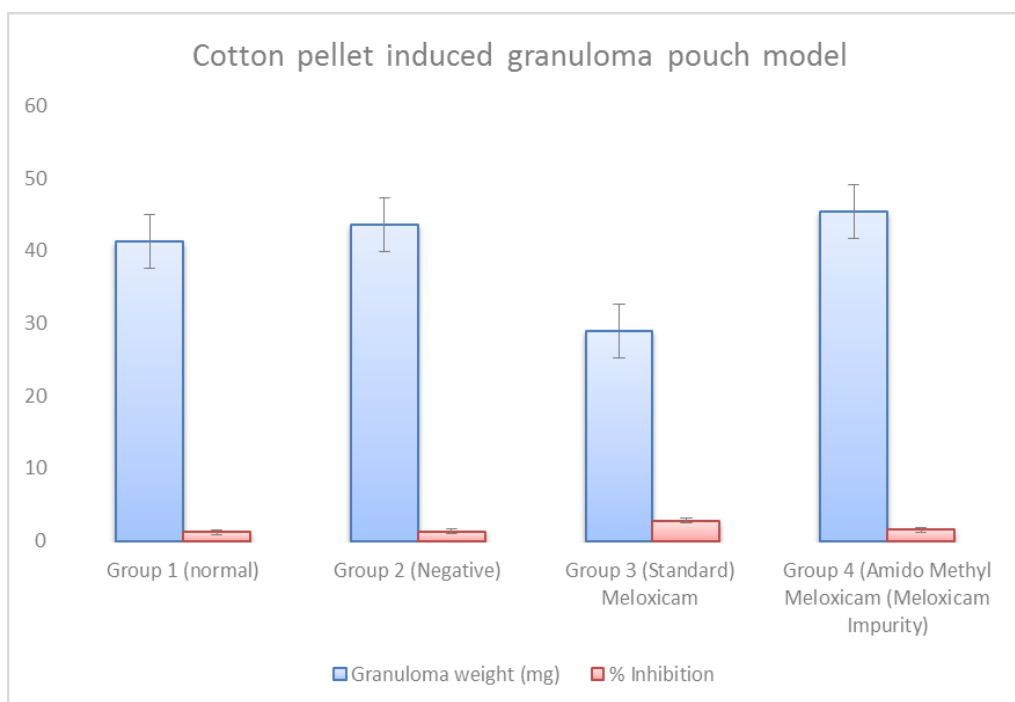
Treatments	Paw thickness in mm				
	0hr	1hr	2hr	3hr	4hr
Group 1 (normal)	1.403 ± 0.02	3.406 ± 0.22	4.906 ± 0.04	6.405 ± 0.05	4.802 ± 0.08
Group 2 (Negative)	1.658 ± 0.03	1.749 ± 0.21	1.868 ± 0.07	1.957 ± 0.11	2.256 ± 0.09
Group 3 (Standard) Meloxicam	1.404 ± 0.05	2.203 ± 0.13	2.904 ± 0.09	3.102 ± 0.13	2.204 ± 0.05
Group 4 (Amido Methyl Meloxicam (Meloxicam Impurity))	1.946 ± 0.03	2.154 ± 0.08	2.648 ± 0.09	2.987 ± 0.11	3.543 ± 0.17



Cotton Pellet-Induced Granuloma Method in Rats

Anti inflammatory activity of ethanolic extract of Organic compounds on Cotton pellet induced granuloma pouch model

Treatments	Granuloma weight (mg)	% Inhibition
Group 1 (normal)	41.24 ± 0.04	1.2 ± 0.09
Group 2 (Negative)	43.58 ± 0.02	1.3 ± 0.07
Group 3 (Standard) Meloxicam	28.94 ± 0.03	2.8 ± 0.02
Group 4 (Amido Methyl Meloxicam (Meloxicam Impurity))	45.42 ± 0.06	1.5 ± 0.06



DISCUSSION

Inflammation is a critical physiological response that occurs in response to many different types of harmful agents, including physical trauma, bacterial infection, chemicals, and physical phenomena, with the ultimate goal of minimising damage and facilitating tissue

healing. Tissue regeneration, immune monitoring, and repair all work better when inflammation is present after damage (Vodovotz et al., 2008). We are protected by the inflammatory response, which releases cells and mediators to eliminate invaders and stop infections.

Meloxicam and its Derivatives inhibited Carrageenan-induced inflammations in rat models, indicating that it has potent anti-inflammatory effects, according to the study's findings.

CONCLUSION

In order to determine the effectiveness of natural substances in reducing inflammation, the carrageenan-induced paw edema model is often used. The current investigation demonstrated that paw edema volume was generated by Carrageenan injection, and that the amount of edema seen was greatest at the 4-hour mark. The edema seen in the acute phase of inflammation was reduced by the Amido Methyl Meloxicam (Meloxicam Impurity).

Amido Methyl Meloxicam (Meloxicam Impurity)'s effects come from its ability to prevent the production of leukotrienes. Amido Methyl Meloxicam (Meloxicam Impurity) restrained Carrageenan-induced inflammations in rodent models, demonstrating that it has powerful anti-inflammatory impacts, concurring to the study's discoveries.

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