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NOTE

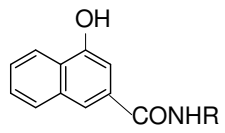
Antiinflammatory Activity of Some Substituted Naphthalenes

SUJATA DEO, FARHIN INAM, R.P. MAHASHABDE* and A.N. JADHAV
Department of Chemistry, Institute of Science, Nagpur-440 008, India
E-mail: rachana_mahashabde@rediffmail.com

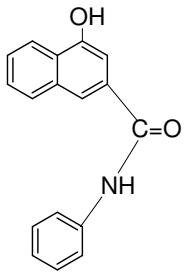
1-Phenyl naphthoic acid, their methyl esters and pericarbonyl lactone systems were evaluated for their antiinflammatory potential. The lactones among the above, were found to be most active in the carrageenen paw edema test.

Key Words: Naphthalenes, Antiinflammatory.

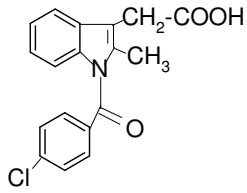
Naproxen is a naphthalene derivative and its structural modification on the basic skeleton was achieved[1,2]. Sheerer and Whitehouse[3] had proposed a hypothetical receptor site for non-steroidal antiinflammatory drug. They had described a similarity in the structure of indomethacin (a standard antiinflammatory drug) and PGE_2[4]. Jiménez *et al.*[5] reported a series of substituted naphthalenes (**I** and **II**) to have similarity with indomethacin (**III**).



(**I**)



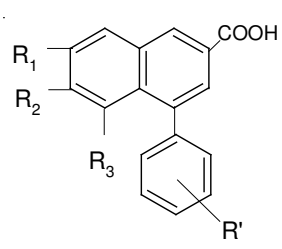
(**II**)



(**III**)

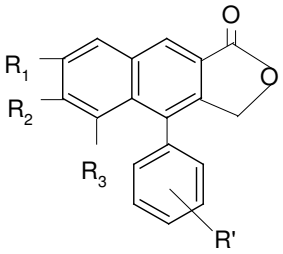
In present work, the antiinflammatory activitives of 1-phenyl naphthoic acid (**1**), their methyl esters (**2**) and pericarbonyl lactones (**3**) synthesized[6] earlier in our laboratory have been reported. *In vivo* and *in vitro* methods are available for the evaluation of antiinflammatory agents[7]. But among the *in vivo* methods the carragenin induced paw edema test (which we have used) is most commonly used for acute antiinflammatory study.

Carragenin induced hind paw edema in rats: The well recognized method of Winter *et al.*[8] was used. Adult albino rats with either sex weighing 100-200 g divided in a group of six were taken. They had free access to food and water except during experimental time.



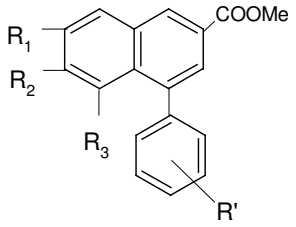
1-Phenyl naphthoic acid

(1)



1-Phenyl naphthalene lactone

(2)



1-Phenyl-3-carbomethoxy naphthalene

(3)

Substitution

For (**1**): a) $R_1 = R_2 = OCH_3$, $R_3 = H$, $R^1 = H$
b) $R_1 = R_2 = R_3 = OCH_3$, $R^1 = H$
c) $R_1 = R_2 = O\text{-}CH_2\text{-}O$, $R_3 = H$, $R^1 = H$
d) $R_1 = OCH_3$, $R_2 = OH$, $R_3 = H$, $R^1 = H$
e) $R_1 = R_2 = R^1 = OCH_3$, $R_3 = H$
f) $R_1 = R^1 = OCH_3$, $R_2 = OH$, $R_3 = H$

For (**2**): a) $R_1 = R_2 = R_3 = OCH_3$, $R^1 = H$
b) $R_1 = R_2 = OCH_3$, $R_3 = H$, $R^1 = H$
c) $R_1 = R_2 = O\text{-}CH_2\text{-}O$, $R_3 = H$, $R^1 = H$

For (**3**): a) $R_1 = R_2 = OCH_3$, $R_3 = H$, $R^1 = H$
b) $R_1 = R_2 = O\text{-}CH_2\text{-}O$, $R_3 = H$, $R^1 = OCH_3$
c) $R_1 = R_2 = R_3 = OCH_3$, $R^1 = H$

All the test drugs (**1**, **2** and **3**) and their substitutes (**a-f**) were freshly prepared in propylene glycol taken as vehicle were injected peritoneally in standard doses. Carragenin was injected in volume of 0.1 M into sub-planter region of right hind paw of all rats. Immediately after injection the edema (foot volume) was increased. The developed edema was measured after 4 h by modified plethysmographic method[9].

The group of six rats used as control received normal saline in dose of 2 mL per kg I.P. The other groups used as standard received indomethacin in dose of 10 mg per kg I.P. or phenyl butazone in dose of 100 mg per kg I.P. and test drugs in dose of 30 mg per kg intraperitoneally. The test drugs and standard drugs were given 0.5 h prior to carragenin. The % reduction in edema was measured after 4 h by plethysomometer.

Calculation of antiinflammatory activity:

$$\text{Antiinflammatory activity} = 100\ (1\text{-}V_t/V_c)$$

where V_t and V_c are the average changes in paw volumes in the test drug and control groups, respectively.

Carragenin induced hind paw method in rats was used to calculate antiinflammatory activity. Carragenin[10] is a mixture of polysaccharides composed of sulphated galactose units and is derived from Irish moss *Chondrous crispus*. The edema which develops in rat paw is a biphasic event. In the initial phase histamine and serotonin are released, and in the second phase prostaglandin like compounds are released.

Pharmacological studies were directed to study the antiinflammatory activity of the test drugs (**1**, **2** and **3**) and their substitutes (**1a-f, 2a-c** and **3a-c**) with regards to their structural (pendant like naphthalene ring) and physiological characteristics. Generally it is observed that non-steroidal antiinflammatory drugs show closely related analgesic and antipyretic activities.

The *in vivo* tests carried out with the test drugs (**1a-f, 2a-c** and **3a-c**) by taking indomethacin as standard showed significant antiinflammatory activity (Table-1).

TABLE-1

Compounds	Relative increase in paw value (± SE)	Percentage activity	Significance
Control	2.4		
Indomethacin (standard)	0.8, 0.008	66.61	P < 0.001
1a	1.3, 0.00486	45.83	P < 0.001
1b	1.2, 0.00649	50.00	P < 0.001
1c	2.0, 0.0539	16.86	P < 0.05
1d	1.2, 0.0365	50.00	P < 0.001
1e	1.04, 0.0757	58.66	P < 0.001
1f	1.36, 0.0357	45.83	P < 0.001
2a	0.88, 0.07	63.33	P < 0.001
2b	1.06, 0.0589	55.83	P < 0.001
2c	1.86, 0.1480	22.50	P < 0.001
3a	0.70, 0.07285	70.83	P < 0.001
3b	0.53, 0.0550	77.92	P < 0.001
3c	1.00, 0.0570	58.83	P < 0.001

Where P stands for probability.

Conclusion

The antiinflammatory activity was calculated by the formula 100 ($1-V_t/V_c$) as above. All the phenyl naphthoic acids (**1a-f**) have shown 45-66 % activity. The esters (**2a-c**) were also found to be active (55-63 % activity) except the 3,4-methylene dioxy substituent. All the pericarbonyl lactones (**3a-c**) were found to be most active (with 58-77 % activity) antiinflammatory agents.

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