INTERNATIONAL JOURNAL OF APPLIED BIOLOGY AND PHARMACEUTICAL TECHNOLOGY

www.ijabpt.com Volume-3, Issue-4, Oct-Dec-2012 Coden : IJABPT Copyrights@2012

ISSN : 0976-4550

Received: 02nd Oct-2011 *Revised: 10th Oct-2012* *Accepted: 11th Oct-2012*

Research Article

ANTI-INFLAMMATORY ACTIVITY OF 3-[(5-SUBSTITUED)-1, 3, 4 OXADIAZOLE-2-YL) METHYL AMINO]-2-METHYL QUINAZOLIN-4(3H)-ONES

*[1]Ramesh Dhani

Department of Pharmaceutical Chemistry

*[1]Oil Technological Research Institute, Jawaharlal Nehru Technological University Anantapur, Andhra Pradesh, India

*Corresponding author: E-mail: dhaniramesh1@gmail.com

ABSTRACT: The process of establishing a new drug is exceedingly complexioned involves the talents of people from a variety of disciplines including Pharmaceutical chemistry, biochemistry, physiology, pharmacology, pharmaceutics and medicine. Quinazolinone is a heterocyclic chemical compound. There are two structural isomers, 2-quinazolinone and 4-quinazolinone, with the 4-isomer being the more common. Various novel classes of structurally different quinazolinones have been designed and synthesized depicting potential interventions such as antibacterial, antifungal, antiviral, anticonvulsant, anti-inflammatory, antihistaminic, anticancer CNS depressant, and so on. All the synthesized quinazolinone derivatives were confirmed preliminarily by M.P and TLC and further all the synthesized compounds were screened for anti-inflammatory activity using Phenyl butazone as the standard and carragennin induced paw oedema model used for anti-inflammatory activity.

Key words: Phenyl butazone, anti-inflammatory activity, Quinazolinone, Anthranilic acid, Ethanol.

INTRODUCTION

Medicinal chemistry is concerned mainly with the organic, analytical and biological aspects of this process, but its people must interact productively with those in the other disciplines. It occupies a strategic position at the interface of chemistry and biology. There is considerable overlap with other disciplines for e.g. Medicinal chemistry and pharmacology both are concerned with mode of action and SAR of drugs. However, this kind of overlap facilities productive interactions in research **(**Indian Pharmacopoeia. Ed 3. 1996).

The present survey aims to achieve the pharmacological properties quinazolinones and their derivatives. Quinazolinone has been considered as a magic moiety possessing myriad spectrum of medicinal activities. Diversity of biological response profile has attracted considerable interest of several researchers across the globe to explore this skeleton for its assorted therapeutic significance (Joshi. Dharti et al., 1997).

Various novel classes of structurally different quinazolinones have been designed, synthesized depicting potential interventions such as antibacterial, antifungal, antiviral, anticonvulsant, CNS depressant, Analgesics and anti-inflammatory, antihistaminic, anticancer and so on. Moreover, the nucleus constitutes an integral structural component in a number of drugs currently employed in several clinical therapies (Gabriel, Schmidt et al., 2000).

EXPERIMENTAL SECTION

Pharmacological Evaluation

All the synthesized quinazolinone derivatives are tested for Anti-Inflammatory activity.

Anti-Inflammatory activity:

Male albino Wister rats weighing 200–250 g, supplied by M: s. B.N. Ghosh & co., Calcutta, India, were placed in cages with wire-net floors in a controlled room temperature 29°C, relative Humidity 60–70% and provided with food and water adlibitum. The animals were deprived of food for 24 h before experimentation but allow free access to tap water throughout. All studies were carried out by using six rats in each group (Junping Kou, Boyang Y et al., 2008).

Carrageenin-induced rat paw oedema

Experimental procedure:

Oedema was induced by subplanter injection of 0.1 ml of 1% freshly prepared suspension of carrageenin into the right hind paws of the rats of four groups of six animals each. The volume of the injected and contra-lateral paws were measured 1,3 and 5 h after induction of inflammation using a plethysmometer according to the method described by Winter et al. (1962) The test groups received the synthesized comounds (200mg/kg), the standard group received phenylbutazone (100 mg:kg), and the control animals received the vehicle only. All the treatments were given intraperitoneally 30 min prior to the injection of carrageenin except for the synthesized compounds .Increase of paw edema thickness was calculated (B.P. Saba, M. Pal et al., 2003).

RESULTS

The results of the anti-inflammatory effect of the 200mg/kg of compounds VIIa,VIIb ,VIIc,VIId, VIIe on carragenin induced oedema in rat's right hind paws are presented in figures2 & 3. There was a gradual increase in oedema paw volume of rats in the control (carragennin treated). However, in the test groups, treated with compounds VIIa, VIIb, VIIc, VIId, VIIe showed a significant reduction in the oedema paw volume. As shown in Table the significant anti-inflammatory effect induced by compounds appeared at 1h and progressively increased. The compounds VIIc & VIIe showed a maximum inhibition of 33.58% & 36.79% respectively at 3rd hour. The anti-inflammatory effect induced by Phenyl butazone progressively increased and reached a maximum (40.49%) at 3rd hour.

Table-1: Physicochemical characterization of synthesized compounds

Compound	Mol. Formula	R^{I}	R^{II}	Mol.Weight	% yield	M.P	R_f Value
VIIa	$C_{18}H_{15}N_3O_2$	H	--	333.12	65%	201°c	0.69
VIIb	$C_{18}H_{15}N_3O_3$	OH	--	349.34	59%	640°c	0.44
VIIc	$C_{18}H_{14}ClN_3O_2$	Cl	--	367.79	51%	571°c	0.73
VIId	$C_{18}H_{13}N_4O_4$	NO_2	--	378.34	65%	654°c	0.68
VIIe	$C_{18}H_{14}ClN_3O_2$	---	Cl	367.79	58%	580°c	0.72

Fig.1 Quinazolinone derivatives VIIa-VIIe

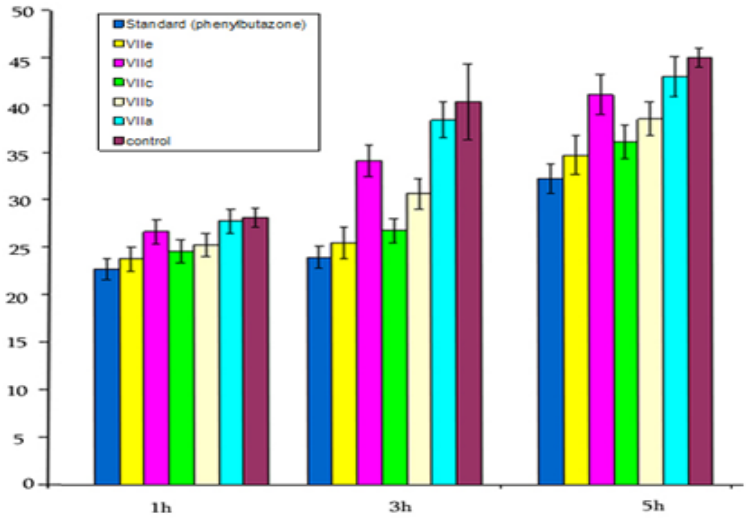

Fig.2 Edema rate % of edema-induced paw in the Carragenin induced Paw-edema method

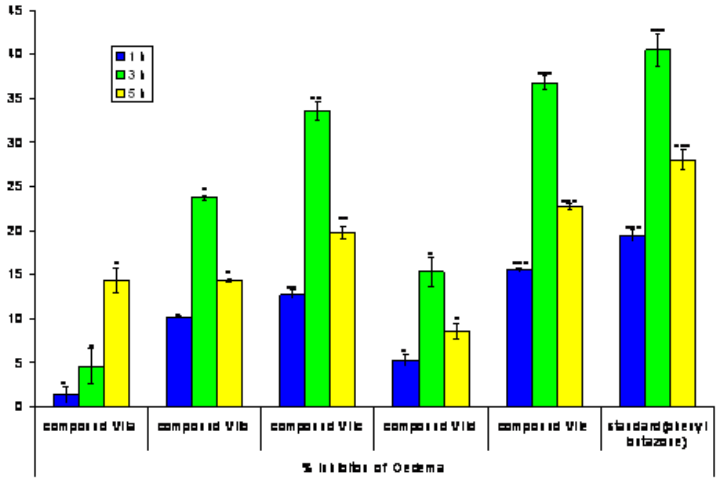

Fig.3 Percentage Inhibition of the edema by compounds VIIa,VIIb,VIIc,VIId,VIIe & standard drug in Carragennin induced paw-edema method

DISCUSSION

The present study establishes the anti-inflammatory activity of the compound VIIa. VIIb, VIIc, VIId, VIIe. The compounds effectively suppressed the inflammation produced by carragenin. It is evident that carragennin induced oedema is commonly used as an experimental animal model of acute inflammation and it is believed to be biphasic of which the first phase is mediated by release of histamine and serotonin in the early phase followed by kinin release and then by prostaglandin in the later phase. But the most significant anti-inflammatory response occurred at the third hour, reduction in paw edema by 33.58% & 36.79% respectively for compound VIIc & VIIe. The standard (phenylbutazone) showed a maximum response at third hour and % inhibition is recorded to be 40.49%.

CONCLUSION

All the synthesized quinazolinone derivatives were confirmed preliminarily by M.P and TLC. and further the synthesized compounds were screened for anti-inflammatory screening using Phenylbutazone as the standard & carragennin induced paw oedema model used for determining anti-inflammatory activity. Among all the compounds VIIe & VIIc which showed good anti-inflammatory activity.

ACKNOWLEDGEMENT

I am indebted to my parents for their inspiration and encouragement given to me during this work with deep appreciation for their determination and enthusiasm at each and every front of my life to transform my dreams into reality.

I am very thankful and prevail age to my deep sense of gratitude to Prof. Dr. K.N. Jayaveera, M.Sc., Ph.D., FIC., FICCP.,FICET.,MISTE, former Director of JNTU-OTRI.

REFERENCES

Indian Pharmacopoeia. ed3. Delhi, The controller of publications.., pp 105-107, 1996.

Gabriel, Schmidt DS. Synthesis of 5- chloro -2- methyl- 3- (5- methylthiazol-2-yl)-4(3H) quinazolinone and related compounds with potential biological activity. *Journal of Heterocyclic Chemistry*. 2000; 37: 725-729.

Minhua Zhou, Honggang Wang, Suolangjiba, Junping Kou, Boyang Y. *Journal of Ethnopharmacology*. 2008; 117: 345-350.

Subhash C. Mandal, Tapan K. Maity, J. Das, B.P. Saba, M. Pal. *Journal of Ethnopharmacology*. 2003; 72: 87-92.

Weddige, J. Prakt. Synthesis and Biological screening of some heterocyclic derivatives of quinazolinones. *Journal of Organic* Chemistry.2005; 36(11):141.

Chen K, Wang K, Kirichian AM, *et al.,* In silico design, synthesis, and biological evaluation of quinazolinone derivatives for alkaline phosphatase-mediated cancer diagnosis and therapy. *Molicular cancer therapy*. 2006; 5(12): 3001-13.

Joshi. Dharti, G. Harish B. Parekh,Synthesis of 2,4-aryl substituted quinazoline 4(3H)one, .*Journal of Medicinal* Chemistry. 1997; 3: 169.

V.Sridharet *et.al.* , Synthesis of novel 4, 6-disubstituted quinazoline deriva- tives,their anti-inflammatory and anti-cancer activity against U937leukemiacells. *European JournalofMedicinalChemistry*. 2007; 14(5): 147-152.

Kunes J, Bazant J, Pour M, Waisser K, Slosarek M, Janota J.Synthesis of quinazoline derivatives with antitubercular activity. *IL Farmaco*. 2000; 55: 725-729.

Andotra, C. S. Langer, T. C. Sumita, D. Biological activity of some Quinazoline and quinazoline derivatives. *Indian Journal of Pharmaceutical Science.*1993; 55: 19-24.

Veluchamy, Muthukumar, agendranPavalarani, Poongavanm. Synthesis, Analgesic and Anti-inflammatory Activities of Some Novel 2, 3-Disubstituted Quinazolin-4(3H) ones. *Biologucal Pharm. Bull*. 2003; 26(4): 557-559.