

CH₃I (3 ml) was added at 40° with stirring, in small lots. It was refluxed for 4 hr, cooled, extracted with CHCl₃ and the product obtained was subjected to the above procedure again till the methylation was complete. It was hydrolysed with aq. H₂SO₄ (7%, 3 ml) as discussed earlier. Aglycone: m.p. 237° (lit. 238–40°)¹², sugar: *R_f* 0.85 (PC, solvent: C, spray: aniline hydrogen phthalate).

ACKNOWLEDGEMENT

One of the authors (SM) is thankful to the CSIR, New Delhi for financial support.

7 September 1982; Revised 4 January 1983

1. Kirtikar, K. R. and Basu, B. D., *Indian Medicinal Plants*, Vol. III Leader Press, Allahabad, 1935, p.910.
2. Hill, A. F., *Economic Botany*, McGraw Hill, New York, 1951, p.245.
3. *The Wealth of India*, 3, C.S.I.R., New Delhi, 1950, p.245.
4. Shankramurthy, P. and Siddiqui, S., *J. Sci. Ind. Res.*, 1948, **B7**, 100.
5. Therasa, Y., Maheswara, M. S., Santappa, M. and Nayudamma. *Lea. Sci. Madras.*, 1977, **746**, 115.

6. Misra, K., Shukla, R. and Trivedi, K. K., *Planta Medica*, 1980, **48**.
7. Malhotra, S. and Misra K., *Phytochem.*, 1981, **20**, 860.
8. Malhotra, S. and Misra, K., *Phytochem.*, (In Press)
9. Malhotra, S. and Misra, K., *Indian. J. Chem.*, (Communicated.)
10. Malhotra, S. and Misra, K., *Phytochem.* 1981, **20**, 2043.
11. Malhotra, S. and Misra, K., *Planta Medica*, (inpress) and 1982, **45**, 143.
12. Seshadri, T. R. and Vasishta, K., *Phytochem.*, 1965, **4**, 317 and 986.
13. Zeisel, S., *Montash.*, 1887, **5**.
14. Shinoda and Ku, *J. Pharm. Soc.*, (Jpn), 1931, **51**, 50.
15. Folin, O. and Wu, H., *J. Biol. Chem.*, 1920, **41**, 367.
16. Purdie, T. and Irvine, J. C., *J. Chem. Soc.*, 1903, **84**, 1021.
17. Mike, O., *Chromatographic methods*, D. Van Nostrand, London, 1961, 75.
18. Malhotra, S. and Misra, K., In *First International Conference on Chemistry and biotechnology of biologically active natural products*, Sofia, Bulgaria, 1981.

QUINAZOLONES AND THEIR PSYCHOPHARMACOLOGICAL ACTIVITY

S. SINGH, M. SHARMA, C. NATH, K. P. BHARGAVA AND K. SHANKER
Department of Pharmacology and Therapeutics, King George Medical College,
Lucknow 226 003, India.

ABSTRACT

Twenty new substituted quinazolones were synthesized and characterized. They were screened for various central nervous system activities. Some compounds have shown potent tranquillizing, anti-depressant and anti-convulsant activities.

INTRODUCTION

EARLIER studies from this laboratory have shown the potentiality of quinazalone moiety for central nervous system (CNS) activity¹. The substitution of position three of quinazalone nucleus plays an important role in imparting CNS activity in quinazolones². We have, therefore, incorporated different moieties via a phenyl bridge at position three to see the effect of these substituents on CNS activity.

EXPERIMENTAL

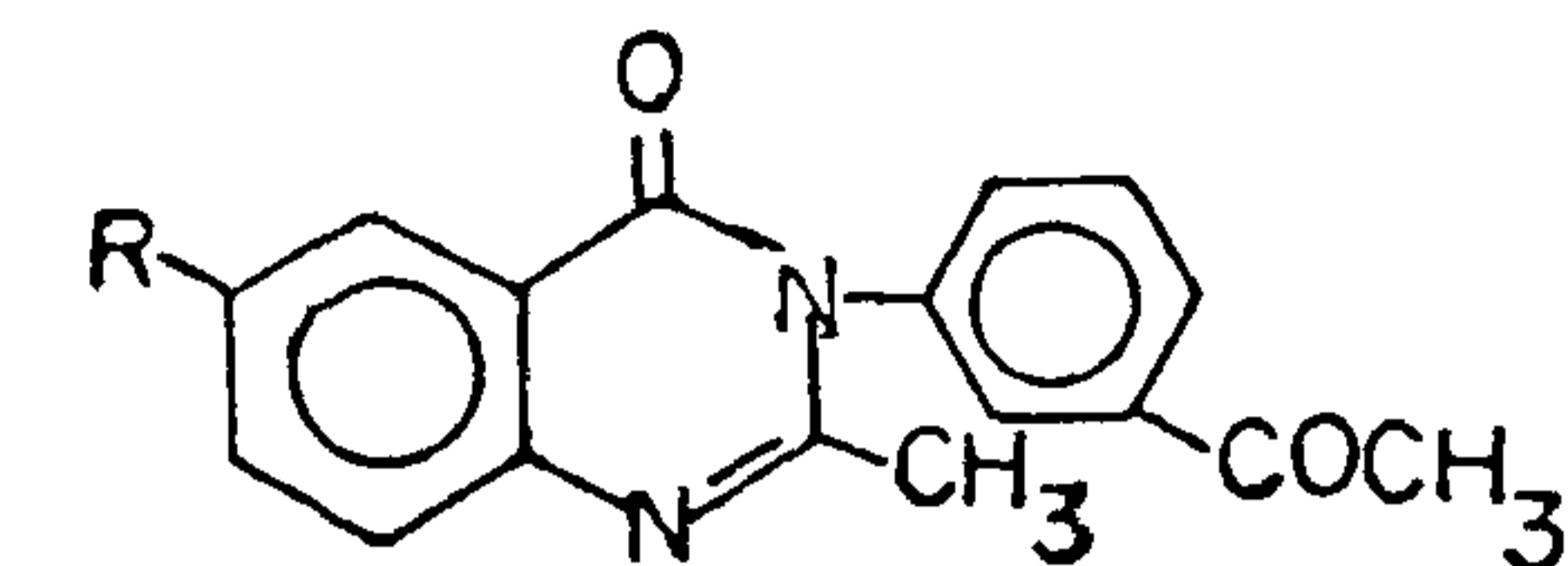
Melting points were determined in open capillary

tubes and are uncorrected. TLC was carried out by employing silica gel G. Mass spectra were recorded on J. M. S. D. 300 focussing spectrometer with J.M.A. 2000 data. 5-Bromo and 5-iodo anthranilic acids were prepared by known methods^{3,4}.

2-methyl-3-(3'- acetyl aryl)-6-substituted 4 (3H) quinazolones

These were prepared by the fusion of substituted acetantraniols (0.01 mole) and m-amino acetophenone (0.01 mole). The resultant jelly-like mass was crystallized with ethanol. Quinazolones thus prepared are reported in table I.

TABLE 1
Characterisation data



Compound	:	R	:	m.p. °C
A	:	H	:	155
B	:	Br	:	125
C	:	I	:	185

(i) All compounds were analysed for nitrogen and the analysis agreed with the theoretical value within the limits of experimental errors.

2-methyl-3- (3'-propionyl substituted piperazino/ amino propio phenyl)-6-substituted-4(3H) quinazolones

To a solution of 2-methyl-3-(3'-acetyl aryl)-6-substituted-4(3H) quinazolone (0.01 mole) in absolute alcohol was added paraformaldehyde (0.01 mole) and different substituted aryl amines or piperazines (0.01 mole) and few drops of hydrochloric acid refluxed for 8-10 hr. The reaction mixture was filtered and the filtrate was concentrated and the solid obtained was washed with petroleum ether and crystallized from alcohol-water. Analytical data are reported in table 2.

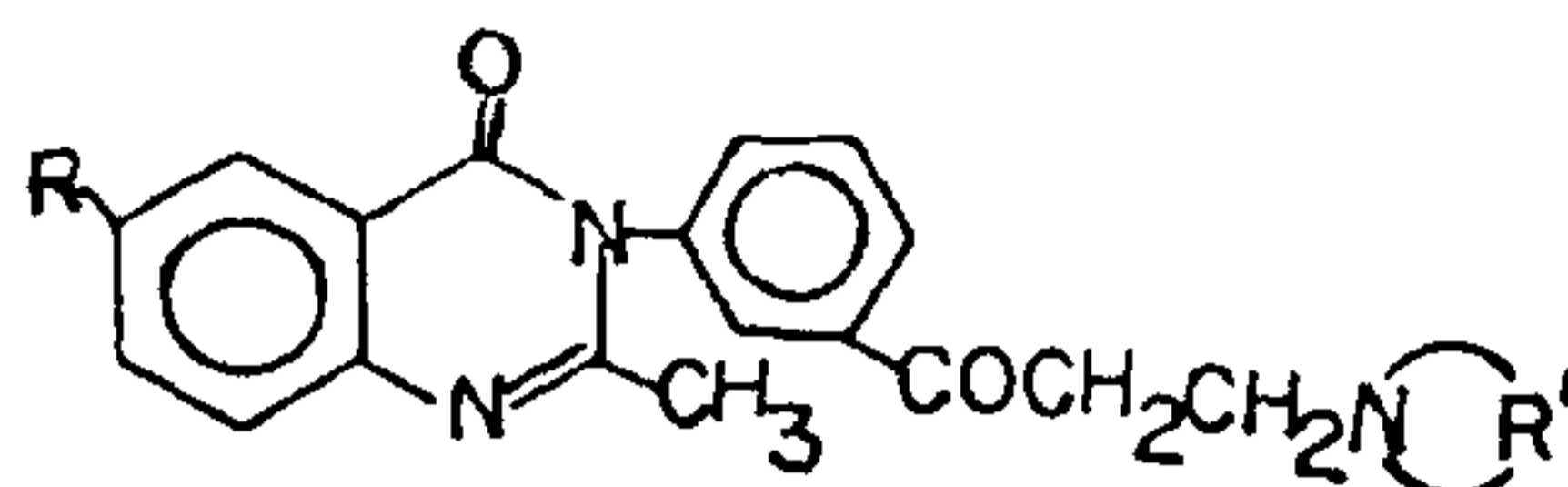
Compound No. 2 of table 2 was used for mass spectroscopic studies. The molecule shows the base peak at m/e 278 (100%) which is due to the cleavage of α -tolyl amino methyl group from the molecular ion and the peak at m/e 120 (48%). Further, the molecule loses its acetyl group attached on the phenyl ring at position 3 of the quinazolone to give the peak at m/e 235 (48%). Fragment A loses a methyl group of position 2 to give the peak at m/e 263 (80%). The other important peaks observed were at m/e 292 and 77.

The fragmentation pattern further confirms structure of the compound.

Pharmacological Studies

These studies were carried out on mice of either sex (20-30 g). Food and water were allowed to the animals *ad libitum*. The compounds were administered at 100 mg/kg i.p. as aqueous suspensions with gum acacia.

TABLE 2
Characterisation data



Compound No.	R	NR ¹	m.p °C
1	H	HN.CH ₂ COOC ₂ H ₅	122
2	H	HN.C ₆ H ₄ .CH ₃ (o)	180
3	H	HN.C ₆ H ₄ .OCH ₃ (p)	115
4	H	HN.C ₆ H ₄ .Cl(p)	110
5	H	HN.C ₆ H ₅	185
6	H	N.C ₆ H ₁₂	119
7	H	HN.C ₄ H ₈ .N.C ₆ H ₄ Cl(p)	117
8	H	HN.C ₄ H ₈ .N.C ₆ H ₄ .CH ₃ (o)	120
9	H	HNC ₄ H ₈ .N.C ₆ H ₄ .OCH ₃ (o)	125
10	H	HN.C ₄ H ₈ .N.C ₆ H ₅	130
11	Br	HN.C ₆ H ₄ CH ₃ (o)	100
12	Br	HN.C ₆ H ₅	118
13	Br	HN.C ₆ H ₄ OCH ₃ (p)	150
14	Br	HN.C ₆ H ₄ .Cl(p)	110
15	Br	HN.C ₄ H ₈ .N.C ₆ H ₅	170
16	Br	HN.C ₄ H ₈ N.C ₆ H ₄ .Cl(p)	140
17	I	HN.C ₆ H ₄ .Cl (p)	100
18	I	HN.C ₆ H ₅	180
19	I	HN.C ₄ H ₈ .N.C ₆ H ₄ .OCH ₃ (o)	150
20	I	HN.C ₄ H ₈ .N.C ₆ H ₄ .OCH ₃ (p)	190

The number of animals in each group was 5, and in the study of foot shock aggression, each group comprised of 5 pairs of mice. Methaqualone was used as standard for comparison. The animals were tested as follows:

(i) *General behaviour*: Spontaneous locomotor activity, awareness, gait, reflexes, reaction of pain, autonomic symptoms (respiration, lacrimation, urination and defaecation) and any gross abnormal symptoms were observed upto 4 hr after administration of the test compounds. Locomotor activity was recorded by placing each group of mice in photoactometer for 15 min. Reaction to pain was tested by electrically heated Eddy's hot plate (Temp. 55°C).

(ii) *Reserpine ptosis*: Reserpine (5 mg/kg i. p.) induced ptosis was scored 0-4/eye according to Rubin *et al*⁶. Reversal of reserpine ptosis indicate anti-depressant activity⁶

(iii) *Foot shock induced aggression (FSA)*: Aggression was elicited by applying electric shock (2mA at a frequency of 5 shocks/sec) to randomly

selected pairs of mice through an aggressometer according to the method described by Anand *et al*⁷. The number of fightings was counted for a duration of 60 sec. Anti aggressive activity represents tranquillizing activity⁶.

(iv) *Metrazole-induced convulsions*: Metrazole (85 mg/kg e.c.) was injected 45 min after test compounds. The animals were watched for convulsion upto 45 min⁸.

(v) *Toxicity Tests*: (i) Acute neurological toxicity tests were done as described by Swinyard *et al*⁸. (ii) Approximate lethal dose 50 (ALD₅₀) value was determined by observing mortality withing 24 hr.

Statistical Analysis

The significance of difference was determined by

applying student's *t* test for mean values, Chi square test (Yates correction) for percent values and Mann Whitney *U* test for non-parametric values (scores).

RESULTS AND DISCUSSION

Compounds C, 1, 2, 7, 9, 10 and 13 significantly reduced the spontaneous locomotor activity (SLA) while compounds 17, 18 and 19 caused significant increase in SLA. Maximum change in SLA occurred 1 to 2 hr after administration of compounds. Awareness was slightly decreased by compounds 1, 7 and 10. None of the compounds showed effect on gait, reflexes, pain-reaction and autonomic system. Reserpine-induced ptosis was significantly reversed by compounds C, 1, 2, 7, 10, 17, 18 and 19. Significant anti-aggressive activity was observed with compounds

TABLE 3
Pharmacological activities

Compound	Spontaneous locomotor activity (SLA) % change	Ptosis Mean score	Foot shock aggression fighting counts/min mean \pm SE	Metrazole convulsions % protection	ALD ₅₀ mg/kg i.p.
Control	—	8.0	3.5 \pm 0.3	0	—
A	(-) 18.7	8.0	3.5 \pm 0.3	0	> 1000
B	(-) 10.7	8.0	3.7 \pm 0.2	0	> 1000
C	(-) 29.3	5.9*	1.5 \pm 0.3*	0	> 1000
1	(-) 40.0*	6.4*	1.7 \pm 0.2*	60*	> 1000
2	(-) 32.0*	6.0*	1.2 \pm 0.2*	60*	> 1000
3	(-) 9.3	8.0	3.0 \pm 0.4	0	> 1000
4	(-) 1.3	7.8	3.0 \pm 0.6	0	> 1000
5	(-) 13.3	8.0	2.5 \pm 0.6	0	750
6	(-) 4.0	8.0	3.2 \pm 0.5	0	> 1000
7	(-) 38.7*	6.2*	1.5 \pm 0.3*	80*	> 1000
8	(-) 2.6	8.0	3.2 \pm 0.2	0	> 1000
9	(-) 28.0*	8.0	3.0 \pm 0.6	20	> 1000
10	(-) 38.7*	6.0*	1.2 \pm 0.5*	60*	> 1000
11	(-) 14.7	8.0	3.5 \pm 0.5	0	1000
12	(-) 8.0	8.0	3.8 \pm 0.2	0	> 1000
13	(-) 21.3*	8.0	3.2 \pm 0.2	0	> 1000
14	(-) 6.0	8.0	2.7 \pm 0.5	0	> 1000
15	(+) 16.0	8.0	3.2 \pm 0.6	0	> 1000
16	(+) 5.3	7.4	2.7 \pm 0.2	0	750
17	(+) 30.7*	5.6*	1.5 \pm 0.2*	0	> 1000
18	(+) 20.7*	5.8*	1.2 \pm 0.5	0	> 1000
19	(+) 26.7*	5.2*	1.7 \pm 0.2*	0	1000
20	(+) 12.0	8.0	2.7 \pm 0.5	0	1000
Methaqualone	(-) 92.6*	8.0	0	100*	—

*Significant difference (< 0.05) from control (+) % increase in SLA from control counts: (—) % decrease in SLA from control counts.

C, 1, 2, 7, 10, 17, 18 and 19. Significant protection against metrazole induced convulsions was shown by compounds 1, 2, 7, and 10. The maximum anti-convulsant activity was exhibited by compound 7. None of the compounds caused acute neurological toxicity in the test doses. ALD_{50} values of the compounds were 1000 mg/kg i.p. in most of the cases.

Compounds 1, 2, 7 and 10 showed tranquillizing (anti-aggressive), anti-depressant (reversal of ptosis) and anti-convulsant activities. It is worthwhile to point out that in general substitution with bromo group, (compounds 11 to 16) did not produce any significant effect. Substitution with iodo group (compounds 17, 18 and 19) showed increase in SLA, contrary to other compounds which caused decrease in SLA. Iodo derivatives showed tranquillizing and anti-depressant activity but were devoid of anti-convulsant activity.

Compound 7 appears to be the most promising in the present series as it showed marked tranquillizing, anti-depressant and anti-convulsant activity with high safety margin. Furthermore, in comparison to methaqualone which possesses marked sedative but no anti-depressant activity, this compound 7 showed anti-depressant activity with less sedation. Thus, the compound 7 may be a promising CNS active compound particularly as tranquillizer-anti depressant agent.

ACKNOWLEDGEMENT

CN is grateful to the Neuropharmacology Unit for financial assistance. MS thanks U.G.C. for financial assistance.

12 August 1982; Revised 20 December 1982

1. Sathi, G., Gujrati, V. R., Agarwal, J. C., Nath, C., Bhargava, K.P. and Shanker, K. *Indian Drugs.*, 1980, 18, 90.
2. Raubach, G. D. and Melamore, W. N., *U. S. Pat.*, 1969, 2, 915, 321.
3. Wheeler, A. S., and Oats, W. M. *J. Am. Chem. Soc.*, 1910, 32, 770.
4. Keemne, C. J. and Hunter, J. H., *J. Org. Chem.*, 1940, 5, 227.
5. Rubin, N., Malone, M. H., Wangh, M. H. and Burke, J. C. *J. Pharmacol. Exp. Therap.*, 1957, 120, 125.
6. Glick, S. D. In *Behavioural pharmacology* (eds) S.D. Glick, S. D. and J. Goldfarb, C. V. Mosby Co., 1976, 339.
7. Anand, M., Gupta, G. P. and Bhargava, K. P. *J. Pharm. Pharmac.*, 1977, 29, 437.
8. Swinyard, E. A., Brown, W. C. and Goodman, L. *S. J. Pharmacol. Exp. Therap.*, 1952, 106, 3, 319.
9. Smith, G. W., *Prog. Med. Chem.*, 1960, 1, 1.

BAIRDIIDAE (OSTRACOD) FROM THE RECENT COASTAL SEDIMENTS OF BHATKAL AREA (KARNATAKA STATE) WEST COAST OF INDIA.

HONNAPPA AND SYED ABRAR

Department of Geology, University of Mysore, Manasa Gangotri, Mysore 576 006, India.

ABSTRACT

Recent coastal sediments of Bhatkal area have yielded four Ostracod species, namely, *Neonesidea cracenticlavula* Maddocks, *Paranesidea cf. P. fracticorallicola* Maddocks, *Bairdoppilata carinata* Kornicker and *Neonesidea schulzi* Hartmann, belonging to genera *Neonesidea* Maddocks¹, *Paranesidea* Maddocks¹, and *Bairdoppilata* Coryell, Sample and Jennings¹ of Bairdiidae family which are described. Taxonomical significance of muscle scar pattern has been discussed with a note on ecology.

INTRODUCTION

SANDY clays and clayey sands of Bhatkal area (figure 1, location map) on micropalaentological investigation have revealed ostracod shells preserved in good condition. The configuration of the muscle scars with reference to shape, position, number and ornamentation have been studied in detail followed by a discussion on the taxonomic significance as estab-

lished by ostracod workers in general and Maddocks¹ in particular. The shell ratios have been employed to interpret the ecology of the sediments of the area under investigation.

Systematic Description: (a) Suborder. Podocopa Sars, 1866 (b) Family. Bairdiidae Sars, 1887 (c) Subfamily. Bairdiinae Sars, 1888 (d) Genus. *Neonesidea* Maddocks, 1869, *Neonesidea cracenticlavula* Mad-