

## ANTI-INFLAMMATORY AND DIURETIC ACTIVITY OF A NEW CLASS OF COMPOUNDS - SCHIFF BASES OF 3-AMINO-2-METHYLQUINAZOLIN 4(3H)-ONES

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( Received on February 8, 1994 )

**Abstract:** Eighteen Schiff Bases of 3-amino-2-methylquinazolin-4(3H)-ones were synthesised and screened for anti-inflammatory and diuretic activity. Anti-inflammatory activity was identified in PNG-1, PNG-13, PNG-14, PNG-15 and PNG-17.

**Key words:** 3-amino-2-methylquinazolin-4(3H)-ones                      diuretic  
schiff bases    anti-inflammatory

### INTRODUCTION

3-amino-2-methylquinazolin-4(3H)-one derivatives are reported to possess a variety of biological properties like hypnotic (1), antifertility (2), and analgesic (3) activities.

A few Schiff bases of 3-amino-2-methylquinazolin-4(3H)-ones were synthesized by us which showed bactericidal activity against both gm +ve and -ve organisms (4). During their Pharmacological screening, some of them showed anti-inflammatory and diuretic activity.

### METHODS

**Lethal dose ( $LD_{50}$ ):** Albino mice (20-25 g) were divided into groups of four each. These were administered 215, 464, 1000 and 2150 mg/kg of drugs intraperitoneally (i.p.) and the observations made for mortality upto 24 hrs. The lethal dose was then taken from the Horn's Table (5).

**Anti-inflammatory activity:** Carrageenan induced paw oedema method (6) was followed. Adult rats of either sex weighing 100-150 g were divided into the groups of five each. Compounds were given orally in suspension using 0.5% (w/v) gum acacia as the suspending agent (100 mg/kg) and the paw volume

determined plethysmographically. After an hour, carrageenan (0.1 ml of 1.0% w/v in normal saline) was injected into the planter aponeurosis of the rat's right hind paw. Volume of the paw was measured after 3 hours of the injection. Percent inhibition of the oedema between the control group and the treated group was calculated and compared with the group receiving standard drug phenylbutazone (30 mg/kg, p.o.).

**Diuretic activity:** Diuretic activity was determined in male adult rats weighing 175-200 g of the Sprague-Dawley strains of CDRI using the method of Kau et al (7) with slight modification as described below.

Animals were fasted overnight with free access to water. They were given normal saline (5 ml/100 g) orally by specially designed cannula. Immediately after the saline loading, each rat was placed in separate hanging metabolic cages and the volume of urine was measured at hourly interval for 5 hrs. Rats with osmolality (micro-osmometer) together with  $Na^+$  and  $K^+$  (flame photometer) level not with normal range, were excluded. The animals were then paired to have similar cumulative values for the urine volume, osmolality and electrolyte levels. Drugs suspended in 0.5% (w/v) gum acacia were administered orally

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(100 mg/kg) (volume of 1 ml/100 g). The urinary bladder was emptied by gentle compression of the pelvic area and pull of the tail and the rats were placed in metabolic cages. After 5 hrs, the bladder was emptied as before and urine collected. Furosemide (50 mg/kg, p.o.) was taken as standard drug for comparison.

The results are expressed in term of percent urine volume excretion taking furosemide activity as 100. One group of the rats served as control.

### RESULTS AND DISCUSSION

The LD<sub>50</sub> of the synthesised compounds ranged between 464-1000 mg/kg. Out of the eighteen Schiff

bases screened a few were found to show anti-inflammatory and diuretic activities.

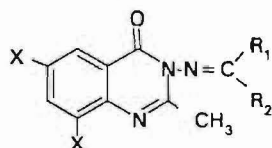
Two compounds namely PNG-14 and PNG-15 (100 mg/kg) showed anti-inflammatory activity comparable with phenylbutazone 30 mg/kg (Table I).

Compound PNG-I, PNG-13 and PNG-17 (100 mg/kg, p.o.) showed appreciable diuretic activity of 72%, 86% and 72% respectively in comparison to furosemide (50 mg/kg, p.o.). No significant effect was observed so far as Na<sup>+</sup> and K<sup>+</sup> concentration or osmolality in urine was concerned.

### ACKNOWLEDGEMENTS

Thanks are due to R.S.I.C., C.D.R.I., Lucknow for Nitrogen analysis of the samples.

## ANTI-INFLAMMATORY AND DIURETIC ACTIVITY OF THE SCHIFF'S BASES (III)



No.	X	R <sub>1</sub>	R <sub>2</sub>	MolFormula	% Nitrogen Cal.(Found) %	Diuretic Activity	Anti- inflammatory	LD <sub>50</sub> mg/kg
PNG-1	H	CH <sub>3</sub>	-C <sub>6</sub> H <sub>5</sub>	C <sub>17</sub> H <sub>15</sub> N <sub>3</sub> O	15.11 (15.04)	72	11	>1000
PNG-2	H	CH <sub>3</sub>	p-C <sub>6</sub> H <sub>4</sub> (OCH <sub>3</sub> )	C <sub>18</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub>	13.68 (13.52)	12	-	825
PNG-3	H	H	-CH=CH-C <sub>6</sub> H <sub>5</sub>	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> O	14.53 (14.50)	12	08	681
PNG-4	H	H	-C <sub>6</sub> H <sub>5</sub>	C <sub>16</sub> H <sub>13</sub> N <sub>3</sub> O	15.97 (16.04)	11	-	>1000
PNG-5	H	C <sub>6</sub> H <sub>5</sub>	-C <sub>6</sub> H <sub>5</sub>	C <sub>22</sub> H <sub>17</sub> N <sub>3</sub> O	12.57 (12.44)	53	27	681
PNG-6	H	CH <sub>3</sub>	p-C <sub>6</sub> H <sub>4</sub> (OH)	C <sub>17</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	14.33 (14.42)	49	-	464
PNG-7	H	CH <sub>3</sub>	p-C <sub>6</sub> H <sub>4</sub> (CH <sub>3</sub> )	C <sub>18</sub> H <sub>17</sub> N <sub>3</sub> O	14.43 (14.34)	20	20	681
PNG-8	H	CH <sub>3</sub>	CH <sub>3</sub>	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O	19.53 (19.47)	17	13	>1000
PNG-9	H	CH <sub>3</sub>	p-C <sub>6</sub> H <sub>4</sub> (NH <sub>2</sub> )	C <sub>17</sub> H <sub>16</sub> N <sub>4</sub> O	19.17 (19.30)	-	07	464
PNG-10	Br	CH <sub>3</sub>	-C <sub>6</sub> H <sub>5</sub>	C <sub>17</sub> H <sub>13</sub> N <sub>3</sub> OBr <sub>2</sub>	9.66 (9.54)	46	11	825
PNG-11	Br	CH <sub>3</sub>	p-C <sub>6</sub> H <sub>4</sub> (OCH <sub>3</sub> )	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> Br <sub>2</sub>	9.05 (9.00)	05	18	681
PNG-12	Br	H	-CH=CH-C <sub>6</sub> H <sub>5</sub>	C <sub>18</sub> H <sub>13</sub> N <sub>3</sub> OBr <sub>2</sub>	9.39 (9.32)	46	32	562
PNG-13	Br	H	-C <sub>6</sub> H <sub>5</sub>	C <sub>16</sub> H <sub>11</sub> N <sub>3</sub> OBr <sub>2</sub>	9.98 (9.81)	86	05	825
PNG-14	Br	CH <sub>3</sub>	p-C <sub>6</sub> H <sub>4</sub> (NH <sub>2</sub> )	C <sub>17</sub> H <sub>14</sub> N <sub>4</sub> OBr <sub>2</sub>	12.45 (12.34)	-	36	562
PNG-15	Br	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	C <sub>22</sub> H <sub>15</sub> N <sub>3</sub> OBr <sub>2</sub>	8.45 (8.39)	-	39	681
PNG-16	Br	CH <sub>3</sub>	p-C <sub>6</sub> H <sub>4</sub> (OH)	C <sub>17</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> Br <sub>2</sub>	9.31 (9.45)	06	03	464
PNG-17	Br	CH <sub>3</sub>	p-C <sub>6</sub> H <sub>4</sub> (CH <sub>3</sub> )	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> OBr <sub>2</sub>	9.35 (9.28)	73	13	>1000
PNG-18	Br	CH <sub>3</sub>	CH <sub>3</sub>	C <sub>12</sub> H <sub>11</sub> N <sub>3</sub> OBr <sub>2</sub>	11.27 (11.39)	40	11	825
Furosemide (50 mg/kg p.o.)						100		
Phenylbutazone (30 mg/kg p.o.)							42	

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