Table II—Comparison of Force Gauge I[a] to Three New Testers[b] over 3 Days[c]

	Slope						Intercept					
	Operator 1			Operator 2			Operator 1			Operator 2		
Tester	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
A	1.03	1.02	1.01	1.01	1.02	1.02	0.061	0.068	0.118	0.103	−0.053	−0.043
B	1.00	0.994	0.988	0.995	0.992	0.990	−0.203	−0.185	−0.159	−0.171	−0.107	−0.091
C	1.00	1.00	1.00	0.999	0.993	0.998	−0.185	−0.168	−0.219	0.002	−0.035	0.017

[a] Dillon force gauge I was used. [b] Heberlein 2E tablet hardness tester. [c] Correlation coefficient for all data was >0.99.

Table III—Comparison of Force Gauge II[a] to Three New Testers[b] over 3 Days[c]

	Slope						Intercept					
	Operator 1			Operator 2			Operator 1			Operator 2		
Tester	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
A	1.05	1.03	1.02	1.04	1.01	1.03	0.087	0.059	0.040	−0.136	−0.017	−0.255
B	1.01	0.992	1.02	1.00	1.00	1.01	−0.031	0.003	−0.191	−0.157	−0.132	−0.143
C	1.01	0.995	1.01	1.01	0.985	0.980	−0.051	−0.142	−0.172	0.049	0.142	0.067

[a] Dillon force gauge II was used. [b] Heberlein 2E tablet hardness tester. [c] Correlation coefficient for all data was >0.99.

II and III). Tables II and III compare the two force gauges with the three new testers, using the kilogram scale, by two independent operators over 3 days. The slopes for all testers on all days were nearly one, and the intercepts did not differ appreciably from zero. The pendulum-type testers showed good day-to-day reproducibility, and there appeared to be no significant operator variability.

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ACKNOWLEDGMENTS AND ADDRESSES

Received June 23, 1975, from the *Pharmaceutical Research and Development Laboratories, Warner-Lambert Research Institute, Morris Plains, NJ 07950*

Accepted for publication September 12, 1975.

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Antimicrobial Agents: Synthesis and Antimicrobial Activity of New Aryloxyalkyl Esters of *p*-Hydroxybenzoic Acid

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Abstract □ Several new aryloxyalkyl esters of *p*-hydroxybenzoic acid were synthesized and screened for *in vitro* antimicrobial activity. Although a few compounds showed low antifungal activity, many possessed appreciable *in vitro* antibacterial activity. However, none of these compounds was active against *Mycobacterium tuberculosis* ($H_{37}Rv$).

Keyphrases □ *p*-Hydroxybenzoic acid—aryloxyalkyl esters synthesized and screened for antibacterial and antifungal activity *in vitro* □ Parabens—synthesized and screened for antibacterial and antifungal activity *in vitro* □ Antibacterial activity—aryloxyalkyl esters of *p*-hydroxybenzoic acid screened □ Antifungal activity—aryloxyalkyl esters of *p*-hydroxybenzoic acid screened

p-Hydroxybenzoic acid esters (parabens) are known to possess antibacterial and antifungal activities and have been used extensively as preservatives (1–3). Aryloxyalkanols such as *p*-chlorophenoxyethanol (*p*-chlorophenoxetol) and 1-phenoxypropan-2-ol (propylene phenoxetol) possess marked *in vitro* antifungal activity (4).

A literature survey showed that only two aryloxyalkyl esters of *p*-hydroxybenzoic acid, namely, 2-phenoxy- and 2-(*o*-chlorophenoxy)ethyl esters, have been synthesized (5). These two esters were used as plasticizers in making films, and no pharmacological activity was reported. Therefore, the continued search for antimicrobial agents (6) prompted the synthesis of compounds that would combine the characteristic features of the forementioned esters as well as aryloxyalkanols with a view to examining antimicrobial activity. These compounds also could possibly act as *p*-hydroxybenzoic acid

and aryloxyalkanols as a result of biotransformations.

The synthesis and antimicrobial activity of several new aryloxyalkyl esters of *p*-hydroxybenzoic acid (Structure I, Scheme I) are reported in this article.

RESULTS AND DISCUSSION

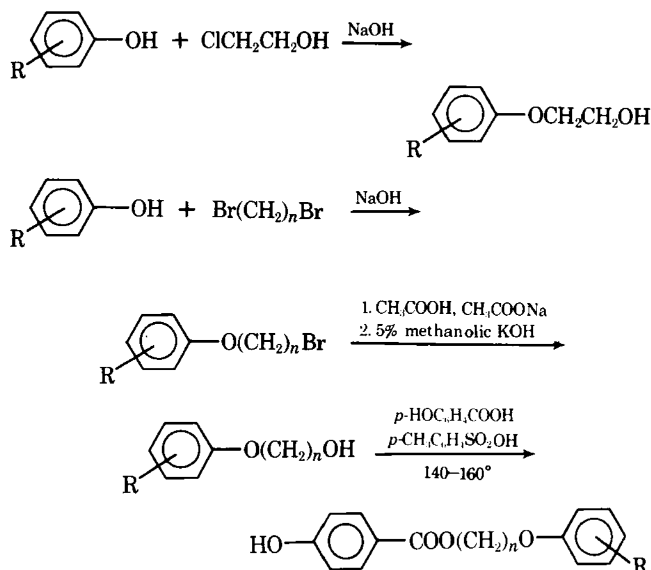
Chemistry—The aryloxyalkyl esters of *p*-hydroxybenzoic acid listed in Table I were synthesized by treating *p*-hydroxybenzoic acid with different aryloxyalkanols at 140–160°, using *p*-toluenesulfonic acid as a catalyst (Scheme I). The intermediate aryloxyethanols were prepared by condensing different phenols with 2-chloroethanol according to the method of Nair and Peacock (7). The remaining aryloxyalkanols were made by converting the respective aryloxyalkyl bromides (8) into the corresponding acetates followed by hydrolysis with methanolic potassium hydroxide.

Fifty-six compounds with varying alkyl chain lengths (n = 2–6) and different aryl functions (Table I) were synthesized and tested *in vitro* for antifungal and antibacterial activities against various fungi and bacteria. All esters were characterized by elemental analyses; IR (mineral oil): 3450 (hydroxyl) and 1700 (ester carbonyl) cm^{-1}.

Biology—All esters were assayed *in vitro* for antibacterial activity against 11 bacteria and for antifungal activity against 10 fungi. The compounds that exhibited significant antibacterial and antifungal activities are listed in Tables II and III. From these data, it can be seen that nine compounds (VII, XX, XXV, XXVII, XXXII, XXXVI, XXXVII, XLII, and XLIV) differed from the rest in showing good activity only against the Gram-negative bacterium, namely, *Pseudomonas aeruginosa.* The *p*-chloro-*m*-tolyloxypentyl ester (XLII) possessed significant activity, inhibiting the growth of this microorganism at 2.5 μg/ml.

Among the compounds showing activity against both Gram-positive and Gram-negative bacteria, the *p*-chloro-*m*-tolyloxybutyl ester (XXIX), the *o*-chlorophenoxypentyl ester (XXXV), and the phenoxyhexyl ester (XLVII) exhibited appreciable activity by inhibiting the growth of five bacteria at 5–25 μg/ml. However, none of these compounds was active against *Escherichia coli, Salmonella typhi, Proteus vulgaris, Vibrio cholerae, Shigella dysenteriae,* or *Mycobacterium tuberculosis* ($H_{37}Rv$) at test concentrations (200 μg/ml).

Only a few compounds exhibited antifungal activity against nine



Scheme I

Table I—Physical Constants of Aryloxyalkyl Esters of *p*-Hydroxybenzoic Acid[a]

HO–C₆H₄–COO(CH₂)ₙO–C₆H₄–R

Compound	R	n	Melting Point[b,c]	Yield[d], %	Molecular Formula	Analysis, % Calc.	Analysis, % Found
I[e]	H	2	109–111°	48	$C_{15}H_{14}O_4$	C 69.77 H 5.42	69.38 5.56
II	2-Cl	2	150–151°	35	$C_{15}H_{13}ClO_4$	C 61.54 H 4.44	61.40 4.80
III	4-Cl	2	152–154°	57	$C_{15}H_{13}ClO_4$	C 61.54 H 4.44	62.04 5.01
IV	2,4-Cl_2	2	123–125°	48	$C_{15}H_{12}Cl_2O_4$	C 55.05 H 3.67	54.50 4.00
V	4-Br	2	156–158°	34	$C_{15}H_{13}BrO_4$	C 53.55 H 3.86	53.90 4.00
VI	2-CH_3	2	115–117°	20	$C_{16}H_{16}O_4$	C 70.58 H 5.88	70.04 6.05
VII	4-CH_3	2	124–125°	21	$C_{16}H_{16}O_4$	C 70.58 H 5.88	70.31 6.36
VIII	3-CH_3, 6-Cl	2	140–142°	35	$C_{16}H_{15}ClO_4$	C 62.65 H 4.90	62.13 5.11
IX	3-CH_3, 6-$CH(CH_3)_2$	2	153–155°	53	$C_{19}H_{22}O_4$	C 72.61 H 7.00	72.40 6.80
X	3-CH_3, 4-Cl, 6-$CH(CH_3)_2$	2	180–181°	60	$C_{19}H_{21}ClO_4$	C 65.42 H 6.02	65.81 6.16
XI	3-NO_2	2	147–149°	27	$C_{15}H_{13}NO_6$	C 59.41 H 4.29	59.12 4.18
XII	4-NO_2	2	170–172°	35	$C_{15}H_{13}NO_6$	C 59.41 H 4.29	59.80 4.60
XIII	H	3	112–114°	26	$C_{16}H_{16}O_4$	C 70.58 H 5.88	70.14 6.05
XIV	2-Cl	3	124–125°	75	$C_{16}H_{15}ClO_4$	C 62.65 H 4.90	63.20 5.18
XV	4-Cl	3	129–130°	15	$C_{16}H_{15}ClO_4$	C 62.65 H 4.90	63.01 5.10
XVI	2,4-Cl_2	3	127–129°	48	$C_{16}H_{14}Cl_2O_4$	C 56.30 H 4.10	56.19 3.98
XVII	2-CH_3	3	113–114°	46	$C_{17}H_{18}O_4$	C 71.32 H 6.29	70.87 6.39
XVIII	3-CH_3	3	111–113°	58	$C_{17}H_{18}O_4$	C 71.32 H 6.29	71.03 6.25

(*continued*)

Table I—*(Continued)*

Compound	R	*n*	Melting Point[b,c]	Yield[d], %	Molecular Formula	Analysis, % Calc.	Analysis, % Found
XIX	4-CH_3	3	89–91°	69	$C_{17}H_{18}O_4$	C 71.32	70.88
						H 6.29	6.50
XX	3-CH_3, 6-Cl	3	117–118°	86	$C_{17}H_{17}ClO_4$	C 63.65	63.65
						H 5.30	5.42
XXI	3-CH_3, 6-$CH(CH_3)_2$	3	98–100°	62	$C_{20}H_{24}O_4$	C 73.16	73.62
						H 7.31	7.50
XXII	H	4	72–73°	50	$C_{17}H_{18}O_4$	C 71.32	71.20
						H 6.29	6.26
XXIII	2-Cl	4	122–124°	60	$C_{17}H_{17}ClO_4$	C 63.65	63.96
						H 5.30	5.72
XXIV	4-Cl	4	121–122°	60	$C_{17}H_{17}ClO_4$	C 63.65	63.86
						H 5.30	5.64
XXV	2,4-Cl_2	4	107–108°	83	$C_{17}H_{16}Cl_2O_4$	C 57.46	57.30
						H 4.50	5.00
XXVI	4-Br	4	112–114°	74	$C_{17}H_{17}BrO_4$	C 55.89	55.80
						H 4.65	4.94
XXVII	2-CH_3	4	120–121°	50	$C_{18}H_{20}O_4$	C 72.00	71.93
						H 6.66	6.62
XXVIII	4-CH_3	4	83–85°	82	$C_{18}H_{20}O_4$	C 72.00	71.64
						H 6.66	6.58
XXIX	3-CH_3, 6-Cl	4	93–94°	60	$C_{18}H_{19}ClO_4$	C 64.60	64.20
						H 5.68	5.88
XXX	3-CH_3, 6-$CH(CH_3)_2$	4	117–118°	30	$C_{21}H_{26}O_4$	C 73.69	73.33
						H 7.60	7.69
XXXI	3-CH_3, 4-Cl, 6-$CH(CH_3)_2$	4	133–134°	76	$C_{21}H_{25}ClO_4$	C 66.93	66.42
						H 6.16	6.63
XXXII	3-NO_2	4	100–101°	30	$C_{17}H_{17}NO_6$	C 61.63	61.18
						H 5.13	4.70
XXXIII	4-NO_2	4	143–144°	15	$C_{17}H_{17}NO_6$	C 61.63	62.00
						H 5.13	5.52
XXXIV	H	5	132–133°	72	$C_{18}H_{20}O_4$	C 72.00	72.60
						H 6.66	6.92
XXXV	2-Cl	5	114–116°	42	$C_{18}H_{19}ClO_4$	C 64.60	64.80
						H 5.68	5.80
XXXVI	4-Cl	5	113–114°	54	$C_{18}H_{19}ClO_4$	C 64.60	64.65
						H 5.68	5.65
XXXVII	2,4-Cl_2	5	109–110°	79	$C_{18}H_{18}Cl_2O_4$	C 58.55	58.40
						H 4.87	4.98
XXXVIII	4-Br	5	112–114°	55	$C_{18}H_{19}BrO_4$	C 57.01	56.90
						H 5.01	5.22
XXXIX	2-CH_3	5	86–88°	55	$C_{19}H_{22}O_4$	C 72.61	73.00
						H 7.00	7.10
XL	3-CH_3	5	75–77°	35	$C_{19}H_{22}O_4$	C 72.61	73.10
						H 7.00	7.24
XLI	4-CH_3	5	102–104°	41	$C_{19}H_{22}O_4$	C 72.61	72.34
						H 7.00	7.09
XLII	3-CH_3, 6-Cl	5	110–112°	70	$C_{19}H_{21}ClO_4$	C 65.42	65.51
						H 6.02	6.34
XLIII	3-CH_3, 6-$CH(CH_3)_2$	5	99–100°	64	$C_{22}H_{28}O_4$	C 74.15	74.40
						H 7.86	7.95
XLIV	3-CH_3, 4-Cl, 6-$CH(CH_3)_2$	5	104–106°	50	$C_{22}H_{27}ClO_4$	C 67.61	67.38
						H 6.92	6.97
XLV	3-NO_2	5	102–103°	76	$C_{18}H_{19}NO_6$	C 62.62	62.80
						H 5.50	5.77
XLVI	4-NO_2	5	114–116°	20	$C_{18}H_{19}NO_6$	C 62.62	62.32
						H 5.50	5.51
XLVII	H	6	89–90°	82	$C_{19}H_{22}O_4$	C 72.61	72.20
						H 7.00	7.03
XLVIII	2-Cl	6	80–82°	48	$C_{19}H_{21}ClO_4$	C 65.42	65.80
						H 6.02	6.42
XLIX	4-Cl	6	105–106°	70	$C_{19}H_{21}ClO_4$	C 65.42	65.90
						H 6.02	6.19
L	2,4-Cl_2	6	62–63°	72	$C_{19}H_{20}Cl_2O_4$	C 59.53	59.80
						H 5.22	5.48
LI	2-CH_3	6	59–61°	55	$C_{20}H_{24}O_4$	C 73.16	73.05
						H 7.31	7.31
LII	3-CH_3	6	84–86°	84	$C_{20}H_{24}O_4$	C 73.16	73.01
						H 7.31	7.44
LIII	4-CH_3	6	94–95°	92	$C_{20}H_{24}O_4$	C 73.16	72.85
						H 7.31	7.12
LIV	3-CH_3, 6-Cl	6	102–103°	51	$C_{20}H_{23}ClO_4$	C 66.21	66.65
						H 6.34	6.53
LV	3-CH_3, 6-$CH(CH_3)_2$	6	100–101°	83	$C_{23}H_{30}O_4$	C 74.59	74.16
						H 8.10	8.29
LVI	3-CH_3, 4-Cl, 6-$CH(CH_3)_2$	6	103–105°	58	$C_{23}H_{29}ClO_4$	C 68.23	68.73
						H 7.16	7.32

[a]These compounds were purified by chromatography over silica gel and eluting with benzene. Final recrystallizations were done with benzene–petroleum ether (bp 40–60°). [b]Analytical sample. [c]Melting points were determined in closed capillary tubes in a sulfuric acid bath and are uncorrected. [d]Based on material that melts within 5° of the analytical sample. [e]The reported melting point (5) is 118°, and it did not improve in this study even after repeated recrystallizations.

Table II—Antibacterial Activities[a] (Minimum Inhibitory Concentration, Micrograms per Milliliter)

Compound	Bacteria				
	Staphylococcus aureus	*Streptococcus faecalis*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	*Agrobacterium tumefaciens*
VII	n.a.	n.a.	n.a.	10	n.a.
XIV	n.a.	n.a.	25	10	25
XV	n.a.	n.a.	200	10	n.a.
XVI	100	25	25	5	200
XVIII	25	n.a.	50	10	25
XIX	25	25	25	25	25
XX	n.a.	n.a.	n.a.	5	n.a.
XXI	25	10	25	5	100
XXII	25	25	50	25	25
XXIII	25	10	25	10	25
XXV	n.a.	n.a.	n.a.	5	n.a.
XXVII	n.a.	n.a.	n.a.	5	n.a.
XXVIII	n.a.	25	n.a.	25	25
XXIX	10	10	25	5	10
XXXII	n.a.	n.a.	n.a.	25	n.a.
XXXV	25	5	5	5	5
XXXVI	n.a.	n.a.	n.a.	5	n.a.
XXXVII	n.a.	n.a.	n.a.	5	n.a.
XXXIX	25	25	25	5	25
XL	25	25	25	5	100
XLI	25	10	25	5	10
XLII	n.a.	n.a.	n.a.	2.5	n.a.
XLIII	n.a.	25	n.a.	5	n.a.
XLIV	n.a.	n.a.	n.a.	5	n.a.
XLV	200	50	25	10	25
XLVII	25	25	10	5	25
XLVIII	25	25	10	5	25
L	n.a.	10	10	5	200
LI	50	25	25	5	n.a.
LII	100	25	50	5	100
LIII	n.a.	200	n.a.	10	200
LIV	n.a.	25	50	25	n.a.
LV	n.a.	50	n.a.	25	n.a.

[a] n.a. = not active up to 200 μg/ml.

Table III—Antifungal Activities[a] (Minimum Inhibitory Concentration, Micrograms per Milliliter)

Compound	Fungi								
	Microsporum canis	*Microsporum gypseum*	*Trichophyton mentagrophytes*	*Trichophyton rubrum*	*Epidermophyton floccosum*	*Candida albicans*	*Cryptococcus neoformans*	*Sporotrichum schenkii*	*Histoplasma capsulatum*
I	50	50	25	50	—	n.a.	100	100	50
VIII	n.a.	n.a.	n.a.	n.a.	—	100	25	n.a.	100
XIV	n.a.	n.a.	n.a.	n.a.	—	n.a.	25	n.a.	n.a.
XV	25	25	n.a.	25	200	n.a.	200	n.a.	n.a.
XVI	n.a.	n.a.	n.a.	n.a.	—	n.a.	7.5	n.a.	n.a.
XVIII	n.a.	100	n.a.	100	—	n.a.	25	n.a.	25
XIX	25	50	50	50	200	n.a.	200	100	200
XXII	n.a.	n.a.	n.a.	n.a.	—	100	25	n.a.	100
XXIII	n.a.	n.a.	n.a.	n.a.	—	n.a.	10	n.a.	n.a.
XXVIII	10	25	50	25	n.a.	n.a.	n.a.	25	n.a.

[a] n.a. = not active up to 200 μg/ml; — = not tested.

of the 10 fungi tested, while none was active against *Aspergillus fumigatus*. The 2-phenoxyethyl ester (I) showed the widest, albeit low, activity, ranging from 25 to 100 μg/ml against seven fungi.

EXPERIMENTAL[1]

3-(*o*-Chlorophenoxy)propyl *p*-Hydroxybenzoate (XIV, Table I)—A mixture of 3-(*o*-chlorophenoxy)propanol (4.1 g, 0.022 mole), *p*-hydroxybenzoic acid (2.75 g, 0.02 mole), and *p*-toluenesulfonic acid (0.1 g) was heated with stirring for 6 hr at 140–160° in an oil bath. The reaction mixture was cooled and extracted with ether (4 × 50 ml), and the ether extract was washed with 5% sodium bicarbonate solution to remove the unreacted acid. The ether layer was then thoroughly extracted with 5% cold sodium hydroxide solution.

The sodium hydroxide extract was neutralized with dilute hydrochloric acid and reextracted with ether (4 × 50 ml). The dried (sodium sulfate) ether extract, on evaporation, gave crude XIV as a brown solid. This solid was purified by chromatography over silica gel, eluting with benzene. An analytically pure sample was obtained as white shining needles by recrystallization from benzene–petroleum ether (bp 40–60°), mp 124–125°, 75% yield; IR[2] (mineral oil): 3450 (hydroxyl) and 1700 (ester carbonyl) cm^{-1}.

All aryloxyalkyl esters of *p*-hydroxybenzoic acid reported in Table I were similarly prepared and characterized by sharp melting points, elemental analyses, and IR spectra.

Biological Methods—The bacteria used were *Staphylococcus aureus*[3] (ATCC 6538), *Streptococcus faecalis*[3] (ATCC 10541),

[1] All compounds were analyzed for their carbon and hydrogen content.

[2] IR spectra were taken in Nujol on a Perkin-Elmer 237 grating IR spectrophotometer.

[3] Obtained from Central Drug Research Institute, Lucknow, India.

Escherichia coli[3] (114), *Salmonella typhi*[3] (115), *Klebsiella pneumoniae*[3] (ATCC 10031), *Pseudomonas aeruginosa*[3] (ATCC 10145), *Agrobacterium tumefaciens*[3] (NRRL B 36), *Proteus vulgaris*[4] (145), *Vibrio cholerae*[4] (ATCC 14033), *Shigella dysenteriae*[4] (ISRC 566/61), and *Mycobacterium tuberculosis*[5] ($H_{37}Rv$).

The fungi used were *Microsporum canis*[3] (VM 200-USPHS), *Microsporum gypseum*[3] (153 CSTM), *Trichophyton mentagrophytes*[3] (A 280-USPHS), *Trichophyton rubrum*[3] (252 CSTM), *Candida albicans*[3] (SKF 2270), *Cryptococcus neoformans*[3] (103), *Sporotrichum schenkii*[3] (107), *Aspergillus fumigatus*[3] (68 LI), *Histoplasma capsulatum*[3] (RNSH Hi 70½ Sydney), and *Epidermophyton floccosum*[5] (HM 300).

Antibacterial Activity—The *in vitro* antibacterial activity was determined by an agar dilution method (9). Twofold serial dilutions of the test compound were prepared in melted tryptone soya agar (oxoid), made into slopes in 18 × 150-mm test tubes. The slopes were streaked with one loopful of an overnight culture of each test organism in tryptone soya broth and incubated for 48 hr at 37°. *M. tuberculosis* was maintained on Lowenstein–Jensen medium.

Antituberculosis activity was tested in Youmans medium (10) following the serial dilution method. To 5 ml of Youmans medium containing the concentrations of the compound, one loopful (4 mm diameter) of 12–14-day-old culture was added. Cells were grown as stationary floating cultures, and growth of cells was followed visually at weekly intervals for 3 weeks.

Antifungal Activity—The compounds were tested for activity by the agar dilution assay method described by Robinson *et al.* (11). The compound under test was diluted in Sabouraud dextrose agar medium, maintained at 50°, in 18 × 150-mm test tubes and slanted. The fungi were streaked across the surface of the slants containing different concentrations of the test compound. The growth was observed visually after 3–14 days, depending upon the test organism.

In all cases, the minimum inhibitory concentration was expressed in terms of micrograms per milliliter at which the growth of the test culture was completely suppressed. A control tube containing the same medium without the test compound was included for each organism tested. Duplicates were maintained for all concentrations.

[4] Obtained from Indian Institute of Experimental Medicine, Calcutta, India.
[5] Obtained from Microbiology & Pharmacology Department, Indian Institute of Science, Bangalore, India.

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ACKNOWLEDGMENTS AND ADDRESSES

Received July 15, 1975, from the **Chemistry Division and the* *‡Microbiology Division, Research & Development Department, Synthetic Drugs Plant, Indian Drugs & Pharmaceuticals Limited, Hyderabad–500 037, India.*

Accepted for publication September 24, 1975.

The authors thank Mr. R. Deshpande and Mr. H. Muralidhar Rao of this Department for microanalyses and spectral data, respectively, and Mr. N. Sridhara Rao and Mr. V. L. V. Ramana Rao for assistance.

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Anti-Inflammatory and Antiproteolytic Properties of 1-(1-Naphthylacetyl)-3-substituted Carbamides

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Abstract □ Several 1-(1-naphthylacetyl)-3-substituted carbamides were synthesized, characterized, and evaluated for anti-inflammatory and antiproteolytic activity. The protection afforded by most of these carbamides against carrageenan-induced edema in rats at a dose of 100 mg/kg ranged from 4.4 to 50%. Some of these carbamides, which showed higher protection against carrageenan-induced edema, were further evaluated for their antigranulation effect against cotton pellet-induced granuloma formation in rats. All carbamides showed a poor degree of protection against granuloma formation. The antiproteolytic activity of these carbamides, as reflected by their ability to inhibit trypsin-induced hydrolysis of the bovine serum albumin, was of a low order and was unrelated to their anti-inflammatory activity.

Keyphrases □ Carbamides, 1-(1-naphthylacetyl)-3-substituted—synthesized, evaluated for anti-inflammatory and antiproteolytic activity □ Anti-inflammatory activity—1-(1-naphthylacetyl)-3-substituted carbamides evaluated □ Antiproteolytic activity—1-(1-naphthylacetyl)-3-substituted carbamides evaluated □ Structure–activity relationships—1-(1-naphthylacetyl)-3-substituted carbamides synthesized and evaluated for anti-inflammatory and antiproteolytic activity

Several arylacetic acids and amides have been reported to be active anti-inflammatory agents (1–6). Earlier studies reported high anti-inflammatory activity for several derivatives of 1-naphthylacetic acid (7, 8) and substituted 1-naphthylacetamide (4, 9). Certain substituted ureas also have been reported to possess anti-inflammatory activity (10). These observations prompted the synthesis of a series of 1-(1-naphthylacetyl)-3-substituted carbamides, which were evaluated for anti-inflammatory activity against carrageenan-induced edema and cotton pellet-induced granuloma formation.