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PREPARATION AND BIOLOGICAL ACTIVITIES OF 2, 3-DIARYLIDENEHYDRAZIDOPHTHALHYDRAZIDE AND RELATED COMPOUNDS

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ABSTRACT:

Phthalazine and its derivatives are compounds with heterocyclic rings which have wide range of applications in medicinal and synthetic chemistry. They exhibit multiple pharmacological activities. Phthalazine is used to lower blood pressure in human. Evaluation of the antimicrobial potential of the newly synthesised compound is an important step in the development of the drug that may be effective against microbial infections and less toxic to the host. Phthalazine derivatives have attracted the attention because of their therapeutic value. The number of phthalazyl hydrazine derivatives are apparently true hypotensive agents of mild potency and reasonable safety. Therefore, researcher has conducted study of synthesis and biological activities of these compounds. The title compounds were synthesised as per the scheme and properly analyzed. Later they were subjected to antimicrobial screening. The results of antimicrobial screening indicates that the phthalhydrazide, it's disodium salt, 2,3-Dihydrazidophthalhydrazide exhibited good antibacterial activity against both types of bacterial species. Thus, phthalazine derivatives have attracted the attention because of their therapeutic value. These are true hypotensive agents of mild potency and reasonable safety. Therefore, researcher has conducted study of synthesis and biological activities of phthalazine derivatives. Some of them have great and promising medicinal value.

Keywords: *Phthalazine, Phthalhydrazide, 2-Phenylphthalhydrazide, Antibacterial, Antimicrobial.*

INTRODUCTION:

The heterocyclic compounds play an important role in the metabolism of all living cells. The important heterocycles such as vitamins, thiamine, riboflavin, nicotinic acid, adenine, biotin, vitamin B12, Vitamin E, chlorophyll (pigment essential for photosynthesis, haemoglobin (Oxygen transporting pigment), purine, and pyrimidine, nucleic acids, uric acid, allantoin, alloxan, histidine, tryptophan, proline, harmones such as kinetin, zeatin, heteroauxin, and histamine contain heterocyclic rings/s in their structures. The medicinal activities of these compounds are due to presence of heterocyclic ring/s in them. Synthesis of some dihydrallazine derivatives and their multiple pharmacological activities were reported by Joshi and Upadhay. Phthalazine and its derivatives is very interesting class of heterocyclic compounds with wide range of applications in medicinal and synthetic chemistry. Phthalazine is used to lower blood pressure in human. A large number of phthalazine derivatives have found

to possess diverse biological and chremiluminescent activities.

Experimental Work

The title compounds were synthesised as per the scheme. The strategy employed for the synthesis of desired 2, 3 Diarylidinehydrazidophthalahydrazides involved the reaction of phthalimide with hydrazine hydrate in ethanol to yield phthalhydrazide I. The 2, 3-Disodium salt of I was N-acetylated with Ethylchloroformate to yield 2,3 Dicarethoxyphthalhydrazide(III). Compound III was condensed with hydrazine hydrate in methanol to yield 2, 3–Dihydrazidophthalhydrazide(IV) and subsequently condensed with substituted aromatic aldehydes to get 2, 3-Diarylidenehydrazidophthalhydrazide(V).

Phthalahydrazide I:

The mixture of phthalimide (14.7 g; 0.1 mole) and hydrazine hydrate (5.0 g; 0.1 mole) in ethanol was refluxed on an oil bath at 120 0C for 20 hours, cooled and the solvent was removed under reduced pressure to obtain the solid which was recrystallized from ethanol to get compound I, yield 12.495 g (85%)

m. p. 336 0C. (Lit. m.p. 334---336 0C)

Analysis:

(Found: C, 59.23; H, 3.69; N, 17.26 C6H6O2 N2

Required C, 59.35; H, 3.70; N, 17.28 %)

IR(KBr): Λmax, 3220 (NH), 1670 (cyclic amide >C=O), 1000 cm-1 (>C=C<)

PMR (CDCl3): δ 6.2 – 7.9 (4 H, m, Aromatic protons)

(2 H, s, broad exchangeable with D2O, CO-NH) ppm.

2, 3-Dicarethoxyphthalahydrazide(III):

The mixture of 2, 3-disodium salt of I (2.08 g; 0,01 mole) and ethyl chloroformate (2.16 g; 0.02 mole) in dry acetone (20 cm3) was refluxed in the presence of anhydrous K2CO3 (0.5 g) on an oil bath for 10 hours, kept overnight to get crystalline product which was filtered and recrystallized from ethanol to furnish (III), yield 1.045 g, (50%), m. p. 137 0C.

Analysis:

(Found: C, 54.87; H, 4.55; N, 9.12 C14H14O6 N2

Required C, 54.90; H, 4.57; N, 9.15 %)

IR(KBr): Λmax, 1765, 1750 (ester >C=O), 1670-1650 cm-1 (cyclic amido and acyclic amido >C=O)

2,3 Dihydrazidophthalahydrazide (IV):

A mixture of III (3.06 g; 0.01 mole) and hydrazine hydrate (1.00 g; 0.02 mole) in methanol (20 cm3) was refluxed on a steam bath for two hours, cooled and the separated solid compound was filtered and further recrystallized from ethanol to yield compound IV. Yield 1.836 g, (60%), m. p. 325 0C.

Analysis:

(Found: C, 43.14; H, 3.57; N, 30.20 C10H10O4 N6

Required C, 43.16; H, 3.59; N, 30.21 %)

IR(KBr): Λmax, 3280, 3100 (NH), 1665-1650 cm-1 broad (cyclic and acyclic amido C=O)

PMR (CDCl3): δ 4.05 – 4.15 (4 H, s, broad, 2 x NH2), 7.7-7.8 (2H, m, Ar-H), 8.1- 8.15 (2 H, s, broad, 2 x CONH) ppm

2, 3- Diarylidenehydrazidophthalhydrazide

To the mixture of IV (0.278 g; 0.001 mole), and p-Chlorobenzaldhyde (0.255 g; 0.002 mole) in methanol, 2-3 drops of acetic acid were added and the reaction mixture was refluxed on a steam bath at 100 0C for five hours, cooled and the solvent was removed under reduced pressure. The solid was recrystallized from ethanol to yield (V), 0.194 g; (70%), m. p. 234 0C.

Analysis:

(Found: C, 55.03; H, 3.03; N, 10.64 C24H8O4 N4Cl2

Required C, 55.06; H, 3.05; N, 10.70 %)

IR (KBr): Λmax, 3350, 3100 (NH), 1670-1650 cm-1 (cyclic and acyclic amido C=O), 1620 cm-1 (C=N)

Similarly, other compounds Va-h were prepared and their physical constant (m. p.), percentage yield, elemental analysis (found and calculated) data have been incorporated in the Table-1

RESULT & DISCUSSION:

Screening of the Antibacterial Activity

The compounds included in the present study such as 3-Arylidenehydrazido-2-phenylphthalahydrazides were tested for their antibacterial activities by Cup Plate Diffusion Method against gram positive and gram negative bacteria. The gram positive bacteria selected for this purpose were *S. Aurius* and *S. Faecalis* and gram negative bacteria were *E. Coli* and *K. Pneumonriiae*.

These bacteria are pathogenic. *Staphylococus Aureus* causes spepsis in wounds and burns. It causes the majority of the acute pyogenic lesions in men. *Staphylococus Aureus* causes tonsilittis, pharyngitis, sinusitis, and pneumonia.

E. Coli causes diarrhoea or gastroenteritis in infants, children and adults. It also causes urinary tract infections, pyogenic infections and septicaemia whereas pseudomonas causes chromic diseases which are in the form of localized or generalized infections. The localized infections are common in wounds, eyes and urinary tract. *Klebsiella pneumonia* causes urinary infections, abscesses, meningitis and septicaemia.

Experimental

The compounds reported in the present study were screened for their antibacterial activities by Kirby-Bauer Disc Diffusion Method. The principle involved in this method is the diffusion of a compound through a solid medium so that a gradient is established, the concentration being highest near the site of application and decreasing with distance.

Table-2: Antimicrobial screening data of 2, 3-Diarylidenehydrazidophthalhydrazide (V) and related compounds

CONCLUSION:

Antimicrobial Screening of 2, 3-Diarylidenehydrazidophthalhydrazide (V) And Related Compounds

The antibacterial activity was evaluated by testing the synthesized compounds at 100 ppm concentration in DMSO against gram positive and gram negative bacteria. The compounds included in this scheme Sr. No. I, II, IV, Va, Vc, Vd, Ve, Vf were found more active than rest of the compounds against bacteria under study. In this series also, the compounds with the substituent pattern R= Chlorophenyl, nitrophenyl, and hydroxyphenyl were found to show significant antibacterial activity. The results of antimicrobial screening indicates that the phthalhydrazide, it's disodium salt, 2,3-Dihydrazidophthalhydrazide have exhibited good antibacterial activity against both types of bacterial species. Thus, these compounds have considerable medicinal value.

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References:

Adrein Albert, Heterocyclic Chemistry an Introduction, Second Edition, p-3, 1968.

Voughan W. R. and Spencer L. Baird, J. Am. Chem. Soc. 68, 1314-16 (1946).

Drain david and Seymour D. E., J. Chem. Soc., 852 (1955).

Joshi H. D., Upadhay P. S.; Baxi A. J., Parikh A. R., Ind. J. Pharm. Sci., 53(3), 78-81 (1991).

https://onlinelibrary.wiley.com/doi/10.1002/aoc.4033

https://en.wikipedia.org/wiki/Phthalazine

https://journals.sagepub.com/doi/full/10.1177/1747519819883840

https://journals.sagepub.com/doi/full/10.1177/1747519819883840

https://en.wikipedia.org/wiki/Phthalazine

Table-1 Physical and Analytical data of 2, 3- Diarylidenehydrazidophthalhydrazide (Va-h)

Compound Sr. No.	R	M. P. (°C)	Yield (%)	Molecular Formula	Elemental Analysis		
					C	H	O
Va	p-Cl.C_6H_4	232	62	$C_{24}H_8O_4N_6Cl_2$	55.00(55.06)	3,03(3.05)	15.00(15.06)
Vb	p-OCH_3.C_6H_4	185	42	$C_{26}H_{22}O_6N_6$	60.00(60.70)	4.20(4.28)	16.30(16.34)
Vc	o-NO_2.C_6H_4	270	40	$C_{24}H_{16}O_8N_8$	52.93(52.94)	2,86(2.94)	20.50(20.59)
Vd	p-$N(CH_3)_2$.C_6H_4	258	44	$C_{28}H_{28}O_4N_8$	62.10(62.22)	5.10(5.18)	20.51(20.74)
Ve	0-Cl.C_6H_4	295	58	$C_{24}H_{16}O_4N_6Cl_2$	54.90(55.06)	2.94(3.06)	15.95(16.06)
Vf	o-OH.C_6H_4	300	55	$C_{24}H_{18}O_6N_6$	59.00(59.25)	3.60(3.68)	17.10(17.28)
Vg	p-OH.C_6H_4	288	40	$C_{24}H_{18}O_6N_6$	59.13(59.25)	3.60(3.70)	17.25(17.28)
Vh	o-OH,m-OCH_3.C_6H_3	205	46	$C_{26}H_{22}O_8N_6$	57.10(57.14)	3.85(4.02)	15.16(15.38)

Table-2: Antimicrobial screening data of 2, 3- Diarylidenehydrazidophthalhydrazide (V) and related compounds

Compound Sr. No.	R	Gram positive bacteria		Gram negative bacteria	
		S. Aureous	S. Faecalis	E. Coli	K. Pneumoniae
I	--	22	20	21	20
II	--	21	18	17	18
III	--	08	09	10	11
IV	--	20	18	19	18
Va	p-Cl.C_6H_4	16	15	14	15
Vb	p-OCH_3.C_6H_4	09	10	07	08
Vc	o-NO_2.C_6H_4	16	17	15	18
Vd	p-$N(CH_3)_2$.C_6H_4	14	12	16	15
Ve	0-Cl.C_6H_4	17	16	14	15
Vf	o-OH.C_6H_4	14	13	15	12
Vg	p-OH.C_6H_4	15	14	13	13
Vh	o-OH,m-OCH_3.C_6H_3	10	11	11	12
Standard Compound	Tetracycline	25	26	25	24

Zone of inhibition in mm:

15-20 mm --- Strong growth inhibitor
09-14 mm --- Moderate growth inhibitor
06-08 mm --- Less growth inhibitor
00-0 mm --- No growth inhibitor