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Contribution in Antimicrobial study of 1,1 bis- {2- hydroxy-3-(1´- phenyl / *H*-5´-aryl-pyrazole 3´-yl) – 5- methyl phenyl} methanes .

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ABSTRACT

Heterocyclic compounds have gained immense importance in human life because of their variety of applications, particularly these compounds have been successfully tested against several diseases and therefore have acquired medicinal importance. Titled Bis-Pyrazoles have been synthesized by condensation of phenyl hydrazine hydrochloride and hydrazine hydrate respectively with Bis-chalcone dibromides in pyridine medium. All compounds have been evaluated for their *in vitro* growth of inhibitory activity against one Gram-positive strain Staphylococcus aureus and three Gram-negative strains like Escherichia coli, Proteus mirabilis and Salmonella typhi using paper disc-method. The culture medium was nutrient agar medium. Most of the titled Bis-pyrazoles are more or less effective against these microorganisms. Hence for treatment of diseases these Bis-pyrazoles can be used by test pathogens only when they do not have any toxic and other side effects.

Keywords: 1, 1 Bis- {2- hydroxy-3-(1´- phenyl / H-5´-Aryl-pyrazol 3´-y1) – 5 methyl phenyl} methanes, Antimiorobial activity.

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INTRODUCTION

Heterocyclic compounds are acquiring more importance in recent years due to the pharmacological activities. Nitrogen, sulphur, oxygen, containing five/six member heterocyclic compounds has occupied enormous significance in the field of drug discovery process. Substituted pyrazole and their analogs have been used as precursors for synthesis of various biologically active.

Pyrazole derivatives possess important pharmacological activities and therefore they are useful material in drug research. The pyrazole nucleus is an important structure in numerous natural and synthetic compounds and in medicinal chemistry. The increasing clinical importances of drug resistant bacterial and fungal pathogens have lent an additional urgency in the field of microbiological research and development of new antimicrobial compounds.

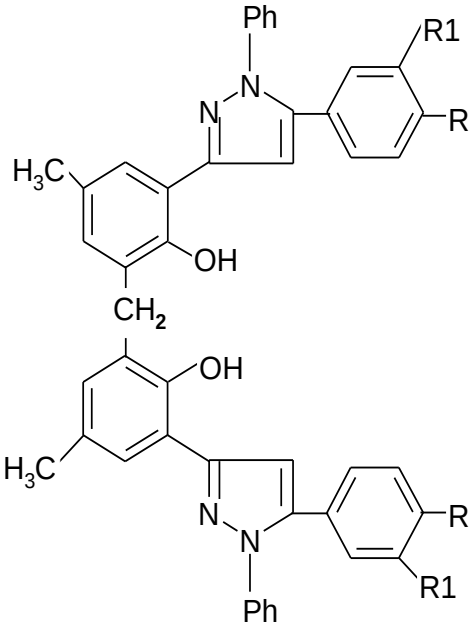
Pyrazole derivatives are use as analgesic[1], anti-viral[2] agents.Pyrazoles are known for their versatile physiological[3], antimicrobial properties[4,5]. Alkyl pyrazole derivatives have been reported as hypolipidemic agents[6]**.** Some phenyl pyrazole are reported as effective antidiabetics[7]. Pyrazoles exhibit wide range of biological ativities like uretic[8], antioxidant[9], antihelmenthetic activities[10], antidepressant[11], anti-inflammatory[12], in addition to fungicidal[13,14] activity. Some of the pyrazole derivatives are reported as antitumor[15] and anticancer[16] activities.

Previously, this laboratory has devoted considerable effort towards the preparation of bis-pyrazolines and bis pyrazoles.The structures of synthesized compounds were assigned on the basis of elemental analysis and spectral study[17] (IR, NMR & UV). The compounds were evaluated for their microbial activity against gram +ve and gram –ve bacteria.

All compounds have been evaluated for their *in vitro* growth of inhibitory activity against different micro-organisms like *Staphylococcus aureus, Escherichia coli, Proteus mirabilis and Salmonella typhi* .The following Bis-pyrazoles were selected for antimicrobial activity,

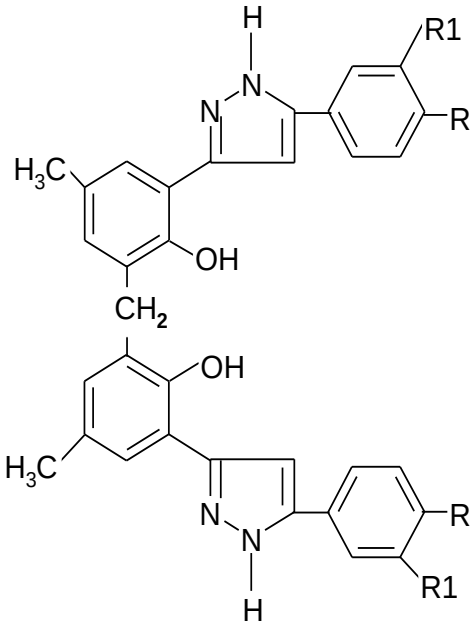
MATERIALS AND MEHOD

The titled compounds were screened *in vitro* for their antimicrobial activity against Staphylococcus aureus, Escherichia coli, Proteus mirabilis and Salmonella typhi. Using paper disc method[18] at concentration of 50µg/ml using DMF as solvent. The culture medium used was nutrient agar medium. After 24± 2 hours of incubation at 37 ± 2 ^{0}C; zones of inhibition were measured in mm and recorded in table 2.



Scheme 1

Compounds (Ia-h)



Scheme 2

Compounds (IIa-h)

Compounds (Ia-h)**:** 1,1 Bis- {2- hydroxy-3-(1′- phenyl -5′-Aryl-pyrazol 3′-y1) – 5 methyl phenyl} methanes,

Compounds (IIa-h)**:** 1,1 Bis- {2- hydroxy-3-(1′- H-5′-Aryl-pyrazol 3′-y1) – 5 methyl phenyl} methanes,

Table 1:- Physical data of 1,1 Bis {2 Hydroxy – 3- [l′-phenyl / H – 5′ – aryl pyrazol -3′ – yl] – 5 – methyl phenyl } methanes. (Ia-h) / (IIa-h)

Compds.	R	R1	M.P.(0 C)	Yield (%)	M.F.	N % Found	Calcu.
Ia	H	H	228-231	75	$C_{45}H_{40}N_4O_2$	8.16	8.38
Ib	OCH_3	H	218-222	74	$C_{47}H_{44}N_4O_4$	7.53	7.69
Ic	OH	OCH_3	265-267	72	$C_{47}H_{44}N_4O_6$	7.12	7.36
Id	OH	H	268	78	$C_{45}H_{40}N_4O_4$	9.62	8.00
Ie	NO_2	H	278	80	$C_{45}H_{38}N_6O_6$	12.47	11.08
If	$N(CH_3)_2$	H	201	85	$C_{49}H_{50}N_6O_2$	10.35	11.14
Ig	H	OCH_3	191-201	70	$C_{47}H_{44}N_4O_4$	7.27	7.69
Ih	OCH_3	OCH_3	235-238	72	$C_{49}H_{48}N_4O_2$	7.03	7.10
IIa	H	H	250-253	78	$C_{33}H_{32}N_4O_2$	9.67	10.85
1Ib	OCH_3	H	246-249	76	$C_{35}H_{36}N_4O_4$	9.61	9.72
IIc	OH	OCH_3	221-224	82	$C_{35}H_{36}N_4O_6$	9.07	9.21
IId	OH	H	255-258	75	$C_{33}H_{32}N_4O_4$	11.33	10.21
IIe	NO_2	H	273	80	$C_{33}H_{30}N_6O_6$	14.22	13.86
IIf	$N(CH_3)_2$	H	173-176	82	$C_{37}H_{42}N_6O_2$	13.22	13.95
IIg	H	OCH_3	186-189	68	$C_{35}H_{36}N_4O_4$	9.32	9.72
IIh	OCH_3	OCH_3	213-215	70	$C_{37}H_{40}N_4O_6$	8.07	8.80

Table 2:-Antimicrobial activities of 1,1 Bis {2 Hydroxy – 3- [l´-phenyl/H –5´ – aryl pyrazole-3´ – yl] – 5 – methyl phenyl } methanes. (Ia-h)/(IIa-h)

Compounds	S.aureus	E.coli	Pr.mirabilis	S.typhi
Ia	-	-	+	-
Ib	-	+ +	+	-
Ic	+	-	-	+ +
Id	+ +	-	+ + +	-
Ie	-	-	+ +	-
If	+ +	+ + +	+ +	-
Ig	+ + +	-	+ +	+ + +
Ih	-	-	+	-
IIa	-	++	+ + +	-
1Ib	-	-	-	-
IIc	-	-	-	-
IId	-	+	-	+
IIe	+	-	+	-
IIf	-	-	+ +	+
IIg	-	-	+ + +	-
IIh	-	-	+ +	-

N.B. :- Zone of Inhibition

-	:	Inactive (Resistance)
+	:	Weak active (Small size zone Inhibition)
++	:	Moderate active
+++	:	Strongly active.

RESULTS AND DISCUSSION:-

The titled compounds were screened for their antimicrobial activities using micro-organisms S.aureus, E.coli, Pr.mirabilis and S.typhi are as follows.

From above table it was observed that, compound **(Ia)** showed weak activity towords Pr.mirabils and inactive towords E-coli , S. aureus&S.typhi.

The compound (**Ib)** howed moderate activity against E-coli, weak activity towards Pr.mirabils, but inactive against S.aureus and S.typhi. The compound (**Ic)** showed moderate activity against S.typhi, weak activity towards S.aureus but inactive against E-coli and Pr. mirabilis. The compound (**Id)** showed strong activity against Pr. Mirabilis moderate activity against S. aureus, but inactive towards E.coli, and S.Typhi. The compound (**Ie)** showed moderate activity against E.coil , Pr. mirabilis but inactive against S. auresus , and S. typhi. The compound (**If)** showed strong activity against E.coli, and moderate activity against S. aureus and Pr.mirabilis and same compound was inactive towards S.Typhi. The compound **(Ig)** showed strong activity against S-aureus and S.typhi moderate activity against Pr. Mirabilis, E-coli and same compound was

inactive against E.coli. The compound **(Ih)** showed weak activity against Pr.mirabilis & inactive against E.coli, S.typhi ,S. aureus. Compound **(II a)** was strongly active towards Pr.mirabilis and moderately active against E.coli and same compound was inactive against S.aureus & S.typhi. The compound **(IIb)** was inactive against all micro-organisms. The compound **(IIc)** was inactive against all micro-organisms. The compound**(IId)** was weakly active against E.coli & S.typhi but inactive towards S.aureus and Pr.mirabilis. The compound **(IIe)** showed weak activity towards S.aureus and Pr.mirabilis but inactive against remaining-E.coli & S.typhi. The compound **(IIf)** showed moderate activity against Pr.mirabilis and weakly active against S.typhi and inactive towards S.aureus and E.coli. The compound **(IIg)** showed strong activity towards Pr.mirabilis inactive against S.typhi,E.coli & S.aureus .The compound **(IIh)** showed moderate activity towards Pr.mirabilis and same compound was inactive towards S.aureus , E.coli & S.typhi .

It has been also found that the antimicrobial activities of the test compounds increases with increase in structure complexity.

From above result it was observed that Bis pyrazoles (titled) were found more or less effective against, Staphylococcus aureus, Escherichia coli, Proteus mirabilis, and Salmonella typhi. Hence those compounds can be easily used.

for treatment of diseases only when they do not have toxic and other side effects.

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