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Antimicrobial and Antifungal Activity of Mn(III) Complexes of 2,5-Dihydroxy-3-undecyl-1,4-benzoquinone Derivative

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Structural modifications of embelin (2,5-dihydroxy-3-undecyl-1,4-benzoquinone), a bioactive compound, were attempted earlier to get various pharmacological profiles. In view of the above reports a new azo derivative of 2,5 dihydroxy-3-undecyl-1,4-benzoquinone with 2-aminobenzothiazole was prepared. The product 6-(2′-benzothiazolylazo) embelin was complexed with Mn(III) chloride, acetate, nitrate and perchlorate. The complexes were screened for antibacterial, antifungal and anthelmintic activities and the complexes were found to exhibit enhanced activity than the ligand.

Key Words: 2-Aminobenzothiazole, 2,5-Dihydroxy-3-undecyl-1,4-benzoquinone, Antibacterial, Antifungal and Anthelmintic activities.

INTRODUCTION

2,5-Dihydroxy-3-undecyl-1,4-benzoquinone (embelin), an orange pigment extracted from the berries of the plant *Embelia ribes burn* is a well known bioactive compound[1-4]. Embelin has wide range of pharmaceutical properties cited in literature. The antifertility and antibacterial activity of embelin have been reported[5,6]. The dried fruit of *Embelia ribes* has been used for a long time in India for the treatment of ring worm and other skin diseases and as an anthelmintic particularly against tapeworm[7-9]. In view of the above report, it was of interest to study the effect of structural modifications on these properties. A new azo derivative of embelin with 2-aminobenzothiazol was prepared. The product 6-(2′-benzothiazolylazo) embelin (H_2ABTE) (**I**) was complexed with Mn(III) using chloride, acetate, nitrate and perchlorate as counter anions. Structure of the compounds were established by elemental analysis, molar conductance, magnetic moment measurements and spectral data (UV & IR). Compounds were screened for antimicrobial and anthelmintic activities.

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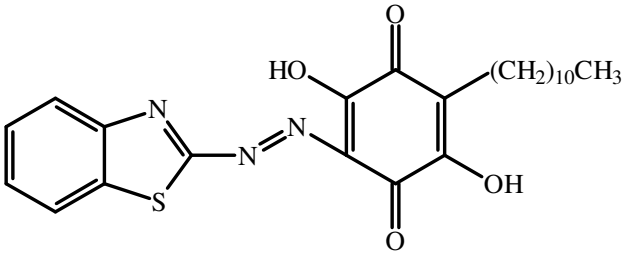

Fig. 1. Strucutre of 6-(2′-Benzothiazolylazo)embelin (H_2ABTE) (**I**)

EXPERIMENTAL

All the chemicals used were of AR grade. Embelin was extracted from the dried powdered berries using ether in a soxhlet apparatus[1,3,5,10]. The extracted product was digested with petroleum ether and recrystallized from absolute alcohol. Mn(III)acetate which was used as starting material for the synthesis of Mn(III) complexes was prepared by reported method[11]. 6-(2′-Benzothiazolylazo)embelin (H_2ABTE) is prepared by the diazotisation of 2-aminobenzothiazole followed by the coupling reaction with ice cold alkaline solution of embelin[12]. Purity was checked by TLC and elemental analysis.

Preparation of complexes

Acetato complex of Mn(III) was prepared by mixing ethanolic solutions of Mn(III)acetate dihydrate and the ligand. The mixture was refluxed and concentrated. The dark brown complex separated was suction filtered, washed and dried in vacuum. Mn(III) complexes with chloride, acetate, nitrate and perchlorate as anions were prepared by adding appropriate salts (KCl, $NaNO_3$, $NaClO_4$) to ethanolic solutions of Mn(III) acetate and the ligand.

The strucutre of the complexes were established by various physicochemical studies such as analytical, spectroscopic, magnetic susceptibility measurements and electrical conductivity data. On the basis of these experimental data, a monomeric distorted octahedral structure was assigned to all complexes of Mn(III) with H_2ABTE.

Biological screening

All the complexes were screened for the antibacterial and antifungal activities. The antibacterial and antifungal activities were tested by agar diffusion cup plate method[13]. The bacteria used for assay were *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Escherichia coli*. The hot nutrient agar solution (20 mL) was poured into sterilized petridishes and allowed to attain room temperature. Seed layer medium which contains the previously grown subculture was lawned into

the petri dishes. Cups were made using sterile borer of 5 mm diameter. To these cups 0.5 mL of the drug solution (500 µg/mL), standard solution were added and allowed to cool for 1 h to facilitate diffusion. The plate was incubated at 37ºC for 48 h. Zone of inhibition around wells were measured. Gentamycin (GTN) was used as the standard (Table-1).

TABLE-1
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES OF H_2ABTE AND ITS Mn(III) COMPLEXES
(ZONE FORMATION IN mm)

Ligands/complexes	SA	EC	KP	PA	AN	CA
Gentamycin	22	15	18	20	16	16
H_2ABTE	14	12	10	10	14	15
$Mn(H_2ABTE)(H_2O)Cl_3$	17	14	15	13	22	20
$Mn(H_2ABTE)(H_2O)(OAc)_3$	15	14	11	11	18	18
$Mn(H_2ABTE)(H_2O)(NO_3)_3$	15	12	14	12	20	19
$Mn(H_2ABTE)(H_2O)(ClO_4)_3$	18	16	16	14	25	22

SA = *S. aureus*; EC = *E. coli*; KP = *K. pneumoniae*; PA = *P. aeruginosa*; AN = *A. niger*; CA = *C. albicans*

Antifungal activity of H_2ABTE and its complexes was tested by the same procedure using Griseofluvin (GFN) as the standard. Fungi used are *A. niger* and *C. albicans* (Table-1). Anthelmintic activity of the complexes at three different concentrations in 2 % Tween 80 were tested using earthworm[14,15]. Mebendazole was used as the standard and control was 2 % Tween 80. 30 mL each of the preparations were taken in petridishes of 3 inch diameter. One earthworm each was put in each dish. The time at which paralysis induced and the lethal time were noted (Table-2).

TABLE-2
ANTHELMINTIC ACTIVITY OF COMPLEX

Group	Dose	Paralysis time (min)	Lethal time (min)
Control	2 % Tween 80	55	80
$Mn(H_2ABTE)(H_2O)Cl_3$	0.5 % in 2 % Tween 80	40	65
	0.75 % in 2 % Tween 80	32	44
	1 % in 2 % Tween 80	17	30
$Mn(H_2ABTE)(H_2O)(OAc)_3$	0.5 % in 2 % Tween 80	42	66
	0.75 % in 2 % Tween 80	33	46
	1 % in 2 % Tween 80	19	35
Mebendazole	0.05 % in 2 % Tween 80	6	22

RESULTS AND DISCUSSION

Screening results reveal that metal chelates are more bacteriostatic and fungitoxic than the chelating agent itself. Enhanced microbial activity of metal chelates over that of ligand can be explained on the basis of Overtone's concept and chelation theory[16,17]. According to this concept lipid membrane that surrounds the cell favours the passage of only lipid soluble materials, due to which liposolubility is an important factor which controls antimicrobial activity. These non-polar lipid membranes hinder the movement of charged metal ions into the cell. On chelation, the polarity of the metal ion will be reduced to a greater extent which in turn increases the lipid solubility. The increase in lipid solubility can enhance the penetration of the complexes into the lipid membrane and interact with the cellular compounds, thereby blocking the normal cell process[18,19]. The toxicological NCS group may be responsible for increased activity of H_2ABTE complexes of Mn(III). It is reported that ligands containing sulphur/or nitrogen donor atoms are likely to be most effective since they increases the liposolubility upon complexation. Complexes showed significant activity towards *S. aureus*. Perchlorato complex exhibit maximum activity. Chloro complex is more active than nitrato complex. The paralysis times in anthelmintic studies indicate that the complexes possess this property and are less than that of mebendazole which is used as the standard.

REFERENCES

1. L.F. Fieser and E.M. Chamberlin, *J. Am. Chem. Soc.*, **70**, 70 (1948).
2. S. Natori, *Chem. Pharm. Bull.*, **12**, 236 (1964).
3. F. Dallacker, *Chem. Ber.*, **105**, 614 (1972).
4. B.S. Joshi and V.N. Kamat, *J. Chem. Soc., Perkin Trans. I*, 327 (1978).
5. S.M. Jain, R. Kant, A.N. Sarin and S.K. Dhar, *Indian J. Chem.*, **28**, 790 (1989).
6. M. Krishnaswami and K.K. Purshotam, *Indian J. Exptl. Biol.*, **18**, 359 (1980).
7. R.N. Chopra, S.L. Nayar, I.C. Chopra, Glossary of Indian Medicinal Plants, CSIR, New Delhi, p. 106 (1956).
8. A.K. Mukerji and V.N. Bhandari, *Indian Med. Gaz.*, **82**, 66 (1947).
9. T. Purandare, *Indian J. Exptl. Biol.*, **17**, 935 (1979).
10. P.G. Sushama and M. Alaudeen, *Asian J. Chem.*, **15**, 366 (2003).
11. O.T. Christensen, *Z. Anorg. Chem.*, **27**, 325 (1901).
12. R.N. Goyal, R. Jarn and S. Tyagi, *J. Indian Chem. Soc.*, **58**, 104 (1981).
13. J. Kaur, S.S. Marwaha and G.S. Sodhi, *J. Indian Chem. Soc.*, **76**, 185 (1999).
14. Anjaneyula and R.P. Rao, *Synth. React. Inorg. Met.-Org. Chem.*, **26**, 257 (1986).
15. L. Mishra and V.K. Singh, *Indian J. Chem.*, **32A**, 446 (1993).
16. A. Kleinzeller, *News Phisiol. Sci.*, **12**, 99 (1997).
17. R. Malhotra, S. Kumar and K.S. Dhindsa, *Indian J. Chem.*, **32A**, 457 (1993).
18. B. Singh, R.N. Singh and R.C. Agarwal, *Indian J. Chem.*, **23A**, 1016 (1984).
19. N. Dharmaraj, P. Viswanathamurthi and K. Natarajan, *Transition Met. Chem.*, **26**, 105 (2001).

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