

## BIOLOGICALLY ACTIVE MIXED-LIGAND COMPLEXES OF RARE-EARTHS

R. C. SHARMA, S. P. TRIPATHI, Km. SUJATA KHANNA AND R. S. SHARMA\*

Chemical Laboratories, Agra College, Agra 282 002, India

## ABSTRACT

1 : 1 : 1, M(III)-HQ-Cat/Pic [where M(III) = La(III), Pr(III), Nd(III), Gd(III) and Dy(III); HQ = 8-Hydroxyquinoline; Pic = 2-Picolinic acid and Cat = Catechol] complexes have been studied potentiometrically and confirmed by IR and elemental analyses. A comparative antifungal activity of these isolated complexes, the involved ligands and the metal ions has been investigated to see the effect on the activity of metal ions and the ligands on chelation. The effect of mixed complexes on some bacteria has also been reported.

## INTRODUCTION

MIXED-ligand complexes of transition metals have been found to possess antifungal and antibacterial<sup>1-2</sup> properties. Recently, Pandey and Joshi<sup>3</sup> have reported the ternary complexes of rare-earths as antibacterials. It was, therefore, considered worthwhile to study more ternary complexes with a view to screening their effect on selected bacteria and fungi.

## MATERIALS AND METHODS

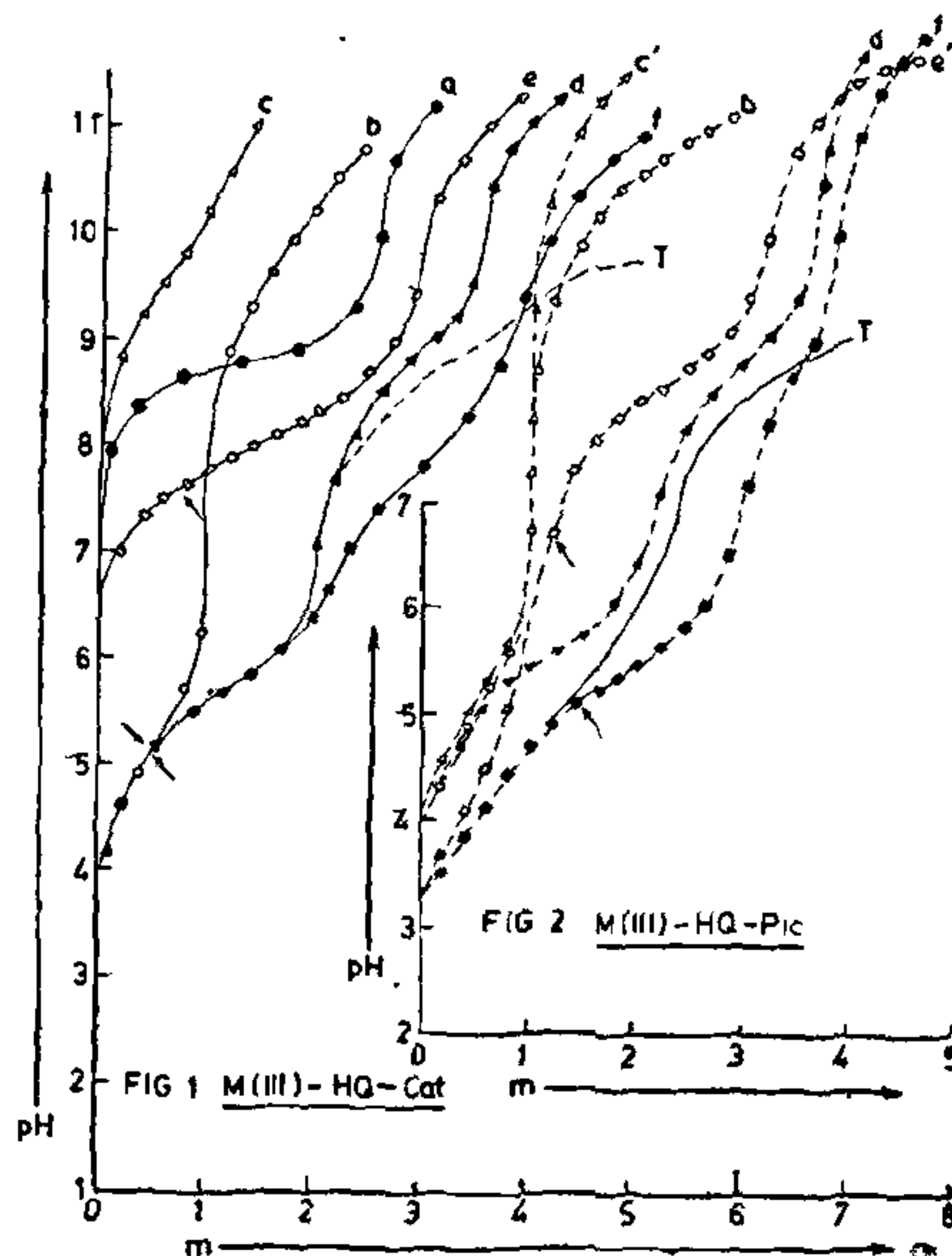
pH-titration was carried out<sup>4</sup> by a Philips pH-meter (PR 9405) and the IR spectra were recorded on Perkin Elmer spectrophotometer IR 4,250 in KBr matrix.

## RESULTS AND DISCUSSION

Curves of similar nature were obtained for the corresponding systems of all the five metals, hence the curves for the systems La(III)-HQ-Cat/Pic have only been discussed for the sake of brevity.

## Binary Systems

Curve *d* (Figs. 1 and 2) depicts the formation of 1 : 3, La(III)-HQ complex<sup>5</sup>, which is further supported by the appearance of a yellow solid at  $m > 1$  and also one more inflection at  $m \sim 4$  due to the precipitation of the remaining metal as its hydroxide. Curve *e* (Fig. 1) exhibits the formation of a neutral 1 : 1, La(III)-Cat hydroxo complex<sup>6</sup>, as indicated by an inflection at  $m = 3$  and the appearance of a green solid. A sharp inflection at  $m = 1$  on the curve *e'* (Fig. 2) is due to the formation of 1 : 1, La(III)-Pic binary complex in the beginning. The appearance of a white solid at  $m > 1$  and other inflection at  $m = 3$  may be ascribed to the disproportionation of the initially formed 1 : 1, complex into 1 : 3, derivative<sup>6</sup> and the remaining metal as its hydroxide.



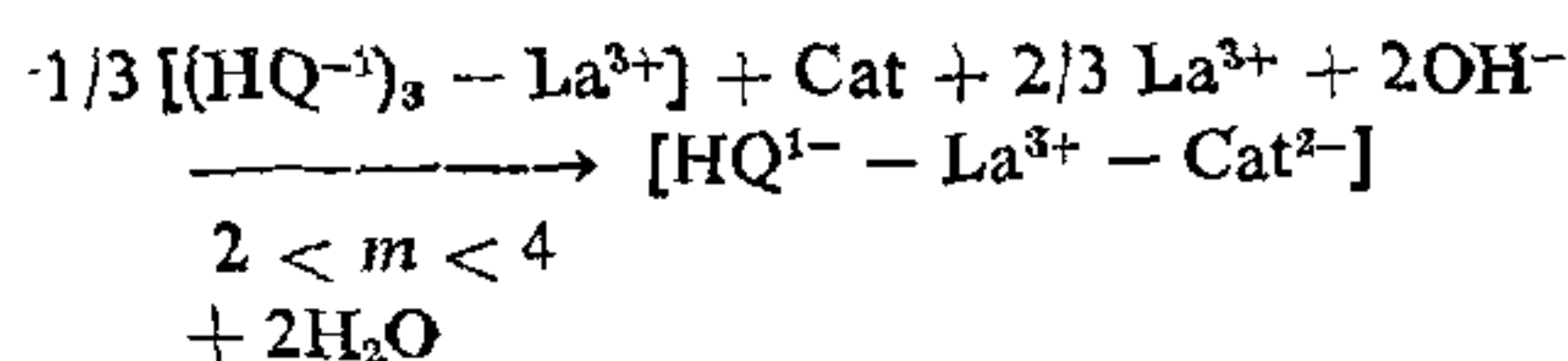
FIGS. 1-2. Fig. 1. Curve *a* = Metal nitrate; *b* = HQ.H<sup>+</sup>; *c* = Cat; *d* = 1 : 1, La(III)-HQ; *e* = 1 : 1, La(III)-cat; *f* = 1 : 1 : 1, La(III)-HQ-cat. Fig. 2. Curve *b* = HQ.H<sup>+</sup>; *c'* = Pic; *d* = 1 : 1, La(III)-HQ; *e'* = 1 : 1, La(III)-pic; *f* = La(III)-HQ-pic → appearance of ppt.; T = theoretical composite curve.

## Ternary Systems

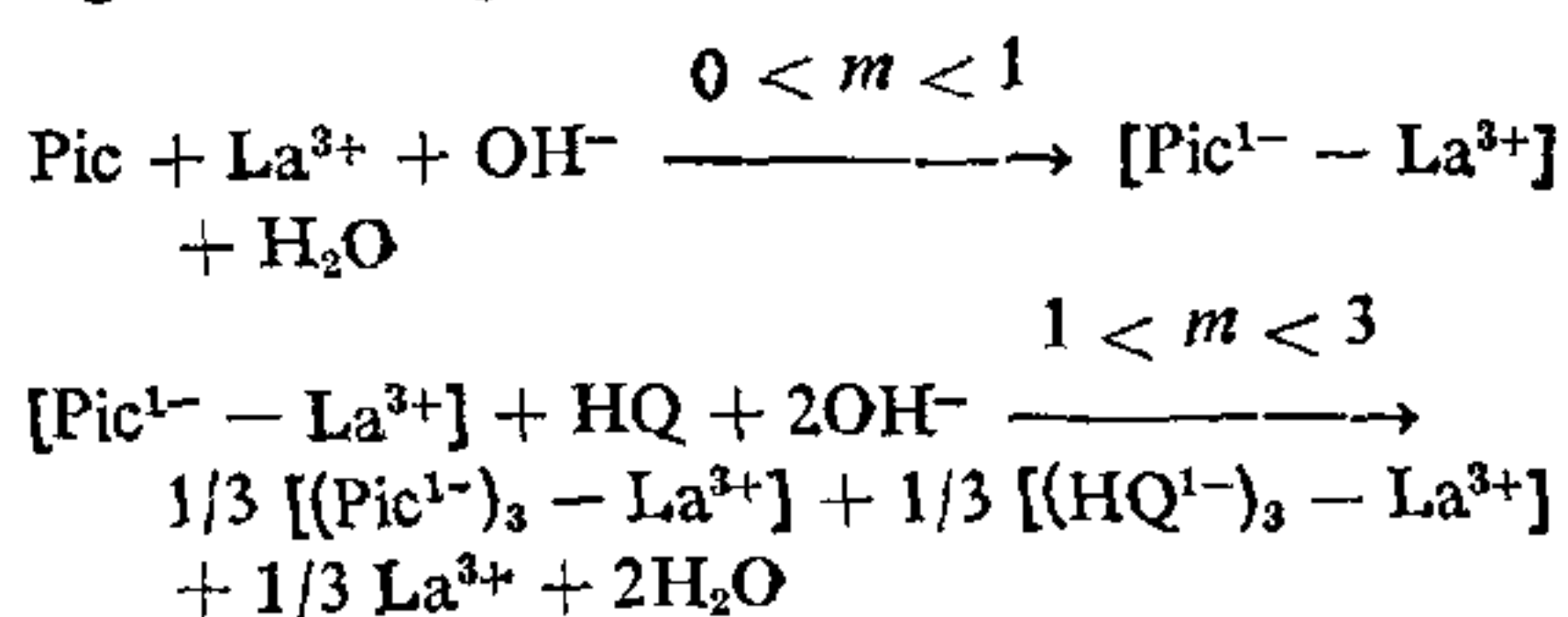
Curve *f* (Fig. 1) illustrates the pH-metric titration of 1 : 1 : 1, La(III)-HQ-Cat ternary system. The initial superimposable nature of this curve to the curve *d* upto  $m \sim 2$  shows the formation of 1 : 3, La(III)-HQ yellow complex in the beginning. The lowering in further buffer region and a sharp inflection

\* Department of Pharmacy, Medical College, Kanpur.

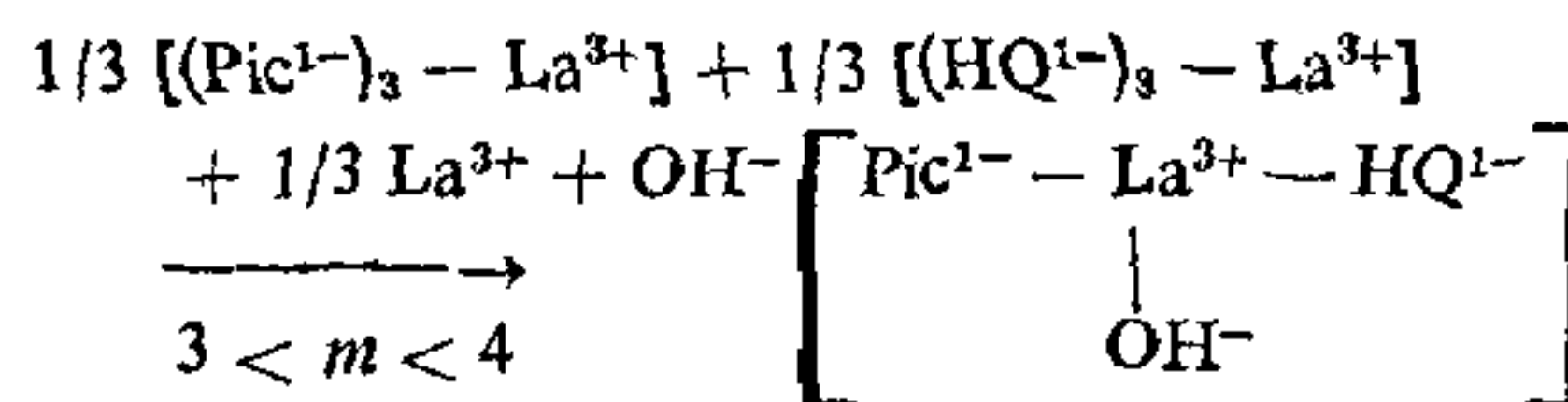
at  $m = 4$  can be attributed to the addition of secondary ligand (Cat.) to the initially formed 1:3, La(III)-HQ complex, resulting in the formation of 1:1:1; La(III)-HQ-Cat mixed ligand species.



Curve  $f$  (Fig. 2) runs almost parallel to the curve  $e'$  upto  $m = 1$ , showing the priority of metal ions to complex with Pic forming 1:1, La(III)-Pic binary complex. The lowering in the pH and a sharp inflection at  $m = 3$  can probably be correlated to the formation of different binary species in the system according to the equation:



The occurrence of one more inflection at  $m \sim 4$  can be ascribed to the addition of a hydroxo group resulting in the formation of 1:1:1 neutral complex.



The formation of the above ternary species is further supported by: (i) The appearance of different coloured solids during titration of ternary systems, (ii) Non-superimposable nature of the theoretical composite curve  $T^7$  with the curve representing mixed-ligand system in the region of mixed ligand complex formation, (iii) IR and elemental analyses of the isolated mixed complexes given in Table I.

IR Studies

The coordination of 8-hydroxyquinoline, 2-picolinic acid and catechol to the metal ions in the above mentioned complexes is further confirmed by the IR

TABLE I  
Elemental analysis

Complex	% of C		% of H		% of N		% of Metal	
	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
La(III)-HQ-Cat. 2H <sub>2</sub> O	41.92	42.18	3.10	3.27	3.67	3.27	32.21	32.51
La(III)-HQ-Pic. H <sub>2</sub> O	40.78	40.93	2.85	2.95	5.98	6.36	31.18	31.55

TABLE II  
Antifungal and antibacterial activity of complexes and free ligands

	Substance	Respective Concentrations, ppm	% inhibition
I. Name of the fungus:			
	HQ/Cat/Pic	200/500/500	88/0/10
	do.	do.	90/0/0
	do.	do.	80/0/0
	La <sup>3+</sup> -HQ-Cat/Pic	200/200	100/100
	do.	200/200	100/100
	do.	200/200	100/100
II. Name of bacteria:			
	La <sup>3+</sup> -HQ-Cat/Pic	200/200	70/85
	do.	do.	100/100

spectral studies. The coordination of the ligands to the metal ion through N and O is supported by the appearance of M-N ( $480\text{ cm}^{-1}$ )<sup>8</sup> and M-O ( $360\text{ cm}^{-1}$ )<sup>8</sup> bands in the IR spectra. The presence of a strong band in the region of  $1170\text{--}1100\text{ cm}^{-1}$  indicate the presence of coordinated oxine<sup>9</sup> molecule. The presence of new bands at  $3400\text{ cm}^{-1}$  and  $1600\text{ cm}^{-1}$  showing the antisymmetric and symmetric OH stretching and HOH bending<sup>10</sup> are due to coordinated water molecules. A sharp band at  $1565\text{ cm}^{-1}$  can be corre-

lated to the  $\text{—C=O}$  stretching of the involved acid and indicates the chelation through carboxylic group.

From Table II one can see that 1:1:1, ternary complexes have been found more active to check the growth of the fungi in comparison to the free metal and involved ligands. The increased activity of these complexes is according to our earlier observations<sup>11</sup> which is again supported by Albert *et al.*<sup>12</sup> and probably depends upon the following facts: (1) due to more liposoluble nature of the ligands on being coordinated with metal ion. (2) To the combined activity effect of the involved ligands and complex. (3) To the comparatively faster diffusion of the metal complex as a whole through the cell membrane of the fungi.

#### ACKNOWLEDGEMENT

Authors feel grateful to Prof. J. P. Tandon, Rajasthan University, Jaipur, Dr. G. K. Chaturvedi and Dr. K. D. Sharma, Agra College, Agra, for their personal interest and to authorities of Agra College, Agra, for providing

necessary laboratory facilities. One of the authors (SPT) is thankful to CSIR, New Delhi, for awarding a Fellowship to him.

1. Sorenson and John, R. J., *J. Med. Chem.*, 1976, 19, 135.
2. Gershon, H. and Parmegiani, R., *Appl. Microbiol.*, 1963, 11, 62.
3. Pandey, S. B. and Joshi, C. R., *J. Inorg. Nucl. Chem.*, 1977, 39, 1289.
4. Tripathi, S. P. and Sharma, R. C., *Chem. Era*, 1978, 14, 81
5. Sharma, R. C. and Tandon, J. P., *Indian J. Chem.*, 1973, 11, 374.
6. Tripathi, S. P., Chaturvedi, G. K. and Sharma, R. C., *Mh. Chem.*, 1978, 109, 283.
7. Caray, G. H. and Martell, A. E., *J. Am. Chem. Soc.* 1967, 89, 2859.
8. Simon, W. and Clerce, T., "Strukturfkalarang Organischer Verbindungen Mit Specktroskopplchon Methoden," *Akademische Verlagsgesellschaft Frankfurt AM MAIN*, 1967.
9. Charles, R. C., Fraiser, H., Friedal, R., Hilland, L. E. and Johnston, W. D., *Spectrochim. Acta*, 1956, 8, 1.
10. Nakamoto, K., *Infra-red Spectra of Inorganic Coordination Compounds*, John Wiley and Sons, New York, 1970, 166.
11. Sharma, R. C. and Tripathi, S. P., *Chem. Era* (In press).
12. Albert, A., Rubbo, S. D., Goldacre, R. J. and Balfour, B. G., *Br. J. Exp. Pathol.*, 1947, 28, 69.

## SYNTHESES OF *ANDROGRAPHIS PANICULATA* FLAVONES

D. K. BHARDWAJ, A. K. GUPTA, RAMESH CHAND AND KUMKUM JAIN

*Department of Chemistry, University of Delhi, Delhi 110 007, India*

#### ABSTRACT

Constitutions assigned to the two flavones isolated from *Andrographis paniculata* as 5-hydroxy-7,8,2'-trimethoxyflavone (I) and 5,2'-dihydroxy-7,8-dimethoxyflavone (II) have been confirmed by their syntheses.

A NEW flavone ( $\text{C}_{18}\text{H}_{16}\text{O}_6$ , m.p.  $186\text{--}87^\circ$ ) isolated<sup>1,2</sup> from *Andrographis paniculata*, on the basis of colour reactions, spectral data<sup>1</sup> and synthetic studies<sup>2</sup> was given the constitution, 5-hydroxy-7,8,2'-trimethoxyflavone (I). This paper now reports the synthesis of I by the modified<sup>3-5</sup> Baker-Verkataraman method which is more convenient and gives good yields. For this purpose, 2-hydroxy-3,4,6-trimethoxyacetophenone<sup>6</sup>

(III) used as the starting material was treated with 2-methoxybenzoyl chloride in the presence of anhydrous potassium carbonate in dry acetone to obtain 2-hydroxy-3,4,6,2'-tetramethoxydibenzoylmethane (IV). Cyclodehydration of the dibenzoylmethane (IV) yielded 5,7,8,2'-tetramethoxyflavone (V) which on selective demethylation gave 5-hydroxy-7,8,2'-trimethoxyflavone (I) identical with the above compound isolated from