THE EFFECT OF METHOXY SUBSTITUTION AND OF CONFIGURATION ON THE THIN-LAYER CHROMATOGRAPHIC BEHAVIOUR OF SOME HETEROYOHIMBINE ALKALOIDS

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INTRODUCTION

PHILLIPSON AND SHELLARD[1,2] have used thin-layer chromatography to distinguish between heteroyohimbine alkaloids and have correlated the behaviour of some new *Mitragyna* alkaloids of unknown stereochemistry with similar alkaloids of known stereochemistry, thus enabling proposals to be made concerning the relative configurations of these new alkaloids. The relative configurations of all these new alkaloids have now been established by means of U.V., I.R., N.M.R. spectra and O.R.D. and C.D. curves[3,4] and these are consistent with the proposals made as a result of the thin-layer chromatographic studies. The behaviour of indole, some methoxyindoles and of 27 heteroyohimbine alkaloids of known stereochemistry on thin layers has now been studied in order to demonstrate the relationship between methoxy substitution in the indole nucleus of heteroyohimbine alkaloids and the configurational differences of the alkaloids and their thin-layer chromatographic behaviour.

METHODS

The details of plate preparation, development of the chromatograms and detection of the alkaloids has previously been described[1]. The thin-layer chromatographic systems are given in Table I.

TABLE I

SOLVENT SYSTEMS FOR THIN-LAYER CHROMATOGRAPHY

Nos.	*Solvent system*	*Thin layer*
1	Benzene–ethyl acetate (7:2)	Silica gel
2	Chloroform–benzene (1:1)	Alumina
3	Chloroform–benzene–diethylamine (1:1:0.001)	Alumina
4	Benzene–ethyl acetate (7:2)	Alumina
5	Ether	Alumina
6	Ether	Silica gel
7	Chloroform–acetone (5:4)	Silica gel
8	Cyclohexane–chloroform (3:7)	Alumina
9	Cyclohexane–chloroform–diethylamine (3:7:0.005)	Alumina
10	Benzene–ethyl acetate–diethylamine (7:2:1)	Silica gel

RESULTS

The results of the separations obtained are shown in Figs. 1–7. The hR_F values given are the average of six separate determinations.

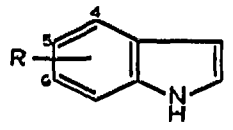
DISCUSSION

The simple indoles examined were: indole (I, R = H), 4-, 5- and 6-methoxyindole (I, R = $-OCH_3$) corresponding to unsubstituted 9-, 10- and 11-methoxy heteroyohimbine alkaloids.

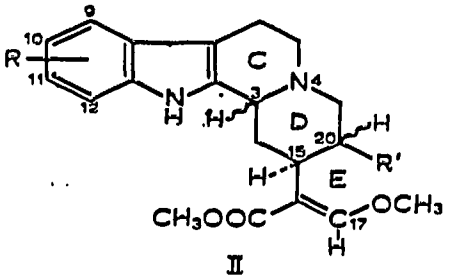
The heteroyohimbine alkaloids examined were of two types depending upon the nature of ring E:

(a) open E ring (E *seco*), (II, R′ = $-CH_2CH_3$ or $-CH{=}CH_2$),

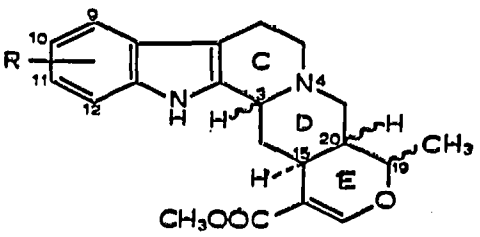
(b) closed E ring (III).



I



II



III

Since all known heteroyohimbine alkaloids possess a C(15)-H α configuration[5] and have asymmetric centres at C(3) and C(20), there are thus four possible configurations[6]:

allo	C(3)-H α	C(20)-H α
epiallo	C(3)-H β	C(20)-H α
normal	C(3)-H α	C(20)-H β
pseudo	C(3)-H β	C(20)-H β.

Other asymmetric centres may exist but all the known E *seco* alkaloids (II) have been shown to possess the same configuration at C(17) (refs. 7, 8), *i.e.* C(17)-H *cis* to the carbomethoxy group. However, the closed E ring alkaloids (III) possess a further asymmetric centre at C(19), *i.e.* CH_3 α or β, so that eight isomers are possible. Further differences in both E *seco* and closed E ring alkaloids are possible because of the presence of methoxy substituents in positions 9, 10, 11 and/or 12 (II, III, R = $-OCH_3$).

The alkaloids examined are listed in Table II.

The effect of methoxy substitution

Fig. 1 shows the behaviour of indole (I, R = H), 4-, 5- and 6-methoxyindole (I, R = $-OCH_3$) in TLC systems Nos. 1–6, no effective separation between these compounds which all have hR_F values 80–100, being observed in systems Nos. 7–10. When arranged in order of decreasing hR_F value, the sequence in all systems is: indole, 4-, 5- and 6-methoxy indole and it might be anticipated that heteroyohimbine alkaloids possessing a common configuration but differing in the aromatic ring by the

TABLE II

HETEROYOHIMBINE ALKALOIDS

Alkaloid	*Type*	*R*	*R'*
1. E seco alkaloids (II)[8–12]			
(a) Corynantheidine	*allo*	H	$-CH_2CH_3$
(b) Mitragynine	*allo*	9-OCH_3	$-CH_2CH_3$
(c) Corynantheine	*normal*	H	$-CH=CH_2$
(d) Dihydrocorynantheine	*normal*	H	$-CH_2CH_3$
(e) Paynantheine	*normal*	9-OCH_3	$-CH=CH_2$
(f) Speciogynine	*normal*	9-OCH_3	$-CH_2CH_3$
(g) Isocorynantheidine	*epiallo*	H	$-CH_2CH_3$
(h) Speciociliatine	*epiallo*	9-OCH_3	$-CH_2CH_3$
(i) Hirsutine	*pseudo*	H	$-CH_2CH_3$
(j) Mitraciliatine	*pseudo*	9-OCH_3	$-CH_2CH_3$
2. Closed E ring alkaloids (III), C(19)-CH_3 α configuration[8,13–17]			
(a) Tetrahydroalstonine	*allo*	H	
(b) Aricine	*allo*	10-OCH_3	
(c) Reserpinine	*allo*	11-OCH_3	
(d) Isoreserpiline	*allo*	10, 11-di-OCH_3	
(e) Ajmalicine	*normal*	H	
(f) Tetraphylline	*normal*	11-OCH_3	
(g) Akuammigine	*epiallo*	H	
(h) Isoreserpinine	*epiallo*	11-OCH_3	
(i) Reserpiline	*epiallo*	10, 11-di-OCH_3	
(j) Isoajmalicine	*pseudo*	H	
(k) Mitrajavine	*pseudo*	9-OCH_3	
3. Closed E ring alkaloids (III), C(19)-CH_3 β configuration[8,13–17]			
(l) Rauniticine	*allo*	H	
(m) Raunitidine	*allo*	11-OCH_3	
(n) Raumitorine	*normal*	10-OCH_3	
(o) Rauvanine	*normal*	10, 11-di-OCH_3	
(p) Isoraunitidine	*epiallo*	11-OCH_3	
(q) Epi-3-rauvanine	*pseudo*	10, 11-di-OCH_3	

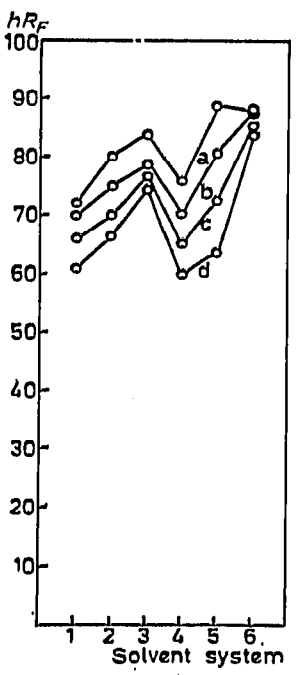


Fig. 1. hR_F values of simple indoles (I): (a) indole (R = H); (b) 4-methoxyindole (R = 4-OCH_3); (c) 5-methoxyindole (R = 5-OCH_3); (d) 6-methoxyindole (R = 6-OCH_3).

absence or presence of 9-, 10- or 11-methoxy substituents would follow the same sequence of hR_F values.

The alkaloids examined on the ten TLC systems show that unsubstituted alkaloids have higher hR_F values than methoxy substituted alkaloids of the same configuration both for E *seco* (II) and closed E ring type (III). In the latter, a 10-methoxy substituted alkaloid has slightly higher hR_F values than an 11-methoxy substituted alkaloid with identical configuration (Fig. 3) so that the behaviour of these two alkaloids is analogous to that of 5- and 6-methoxyindole. Fig. 7 shows that the effect of a second methoxy substituent in ring A is to reduce further the hR_F value.

Hence it is to be expected that heteroyohimbine alkaloids of the same configuration would show decreasing hR_F values in the order: no substitution, 9-, 10-, 11-methoxy substitution and dimethoxy substitution, successively.

The effect of configuration on hR_F values of E seco alkaloids

Fig. 2 shows the behaviour of ten E *seco* alkaloids of known configuration on

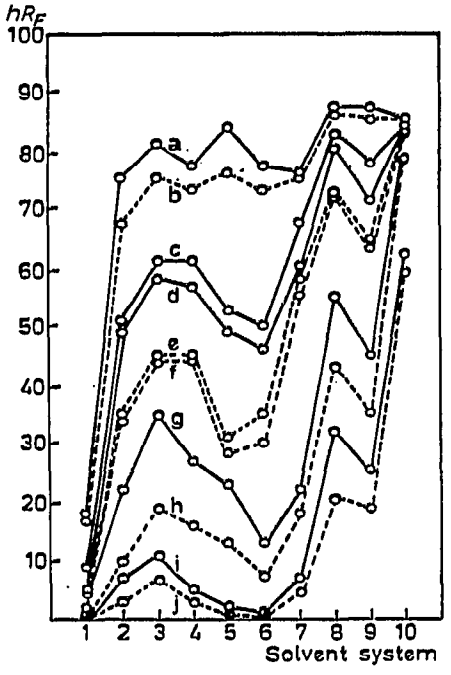


Fig. 2. hR_F values of E *seco* alkaloids (II): (a) corynantheidine (R = H, R′ = $-CH_2CH_3$, *allo*); (b) mitragynine (R = 9-OCH_3, R′ = $-CH_2CH_3$, *allo*); (c) corynantheine (R = H, R′ = $-CH{=}CH_2$, *normal*); (d) dihydrocorynantheine (R = H, R′ = $-CH_2CH_3$, *normal*); (e) paynantheine (R = 9-OCH_3, R′ = $-CH{=}CH_2$, *normal*); (f) speciogynine (R = 9-OCH_3, R′ = $-CH_2CH_3$, *normal*); (g) isocorynantheidine (R = H, R′ = $-CH_2CH_3$, *epiallo*); (h) speciociliatine (R = 9-OCH_3, R′ = $-CH_2CH_3$, *epiallo*); (i) hirsutine (R = H, R′ = $-CH_2CH_3$, *pseudo*); (j) mitraciliatine (R = 9-OCH_3, R′ = $-CH_2CH_3$, *pseudo*). ——— unsubstituted indole, – – – methoxy substituted indole.

ten TLC systems. PHILLIPSON AND SHELLARD[2] have previously suggested that six of these alkaloids could be arranged in order of decreasing hR_F value in the sequence *allo*, *normal*, *epiallo* and *pseudo*. They also suggested that hirsutine, a new *Mitragyna* alkaloid, probably possessed a *pseudo* configuration (i, II, R = H, R′ = $-CH_2CH_3$) following a comparison of its behaviour with the six E *seco* alkaloids on these ten TLC systems. This has recently been confirmed on the basis of physical and spectral

data[4]. Isocorynantheidine (g, II, R = H, R = $-CH_2CH_3$, *epiallo*) falls into sequence between *normal* and *pseudo* compounds having hR_F values higher than speciociliatine (h, II, R = 9-OCH_3, R' = $-CH_2CH_3$, *epiallo*) and lower hR_F values than speciogynine (f, II, R = 9-OCH_3, R' = $-CH_2CH_3$, *normal*). Corynantheine (c, II, R = H, R' = $-CH=CH_2$, *normal*) and paynantheine (e, II, R = 9-OCH_3, R' = $-CH=CH_2$, *normal*) have hR_F values intermediate to those of corynantheidine (a, II, R = H, R' = $-CH_2CH_3$, *allo*) and mitragynine (b, II, R = 9-OCH_3, R' = $-CH_2CH_3$, *allo*) and the *epiallo* alkaloids isocorynantheidine and speciociliatine. Although it has been shown that a methoxy substituent lowers the hR_F value it appears that much greater changes in hR_F value are obtained by alteration of configuration. Thus when the ten E *seco* alkaloids are arranged in order of decreasing hR_F values they are in the sequence *allo*, *normal*, *epiallo* and *pseudo*, a 9-methoxy substituted alkaloid having a lower hR_F value than its corresponding unsubstituted alkaloid.

The effect of the presence of a vinyl group instead of an ethyl group at C(20) (II, R' = $-CH=CH_2$ or $-CH_2CH_3$) on the hR_F values of E "seco" alkaloids

Only two alkaloids with C(20) vinyl groups were available, both being *normal* compounds. Corynantheine (c, II, R = H, R' = $-CH=CH_2$, *normal*) has hR_F values slightly higher than the corresponding alkaloid with α C(20) ethyl group, dihydrocorynantheine (d, II, R = H, R' = $-CH_2CH_3$, *normal*). Paynantheine (e, II, R = 9-OCH_3, R' = $-CH=CH_2$, *normal*) behaves in a similar way having hR_F values slightly higher than the corresponding alkaloid, speciogynine (f, II, R = 9-OCH_3, R' = $-CH_2CH_3$, *normal*). Therefore it would appear that the presence of a vinyl group at C(20) instead of an ethyl group tends to raise the hR_F values but the effect is less marked than the presence or absence of a methoxy group or of a configurational change (Fig. 2).

The effect of configuration on the hR_F values of closed E ring alkaloids

Seventeen closed E ring alkaloids of known configuration were examined on the ten TLC systems (Figs. 3–7).

(*a*) *C(19)-CH_3 α configuration.* Six closed E ring alkaloids of known stereochemistry, possessing a C(19)-CH_3 α configuration, have previously been examined[2] and the sequence in order of decreasing hR_F value found to be *allo*, *normal* and *epiallo*. By comparison of the TLC behaviour with these six alkaloids it was proposed that mitrajavine, a new *Mitragyna* alkaloid probably possessed a *pseudo* configuration[2]. This was because mitrajavine had hR_F values lower than any of these six alkaloids of known configuration and it was argued that the closed E ring alkaloids could be arranged in the same order of decreasing hR_F value as the E *seco* alkaloids. However, a basic assumption for this argument was that mitrajavine possessed the same configuration at C(19) as the other six alkaloids, *i.e.* C(19)-CH_3 α. The configuration of mitrajavine has now been established by means of U.V., I.R., N.M.R. spectra and O.R.D., C.D. curves as 9-methoxy-3-isoajmalicine[18,19] (k, III, R = 9-OCH_3, *pseudo*).

The behaviour, in the ten TLC systems, of these seven closed E ring alkaloids with C(19)-CH_3 α configuration is illustrated in Fig. 3, together with two other alkaloids (akuammigine[20] and isoajmalicine) which have recently become available to us. Akuammigine (g, III, R = H, *epiallo*) has hR_F values higher than the corresponding 11-methoxy substituted alkaloid, isoreserpinine (h, III, R = 11-OCH_3, *epiallo*) and

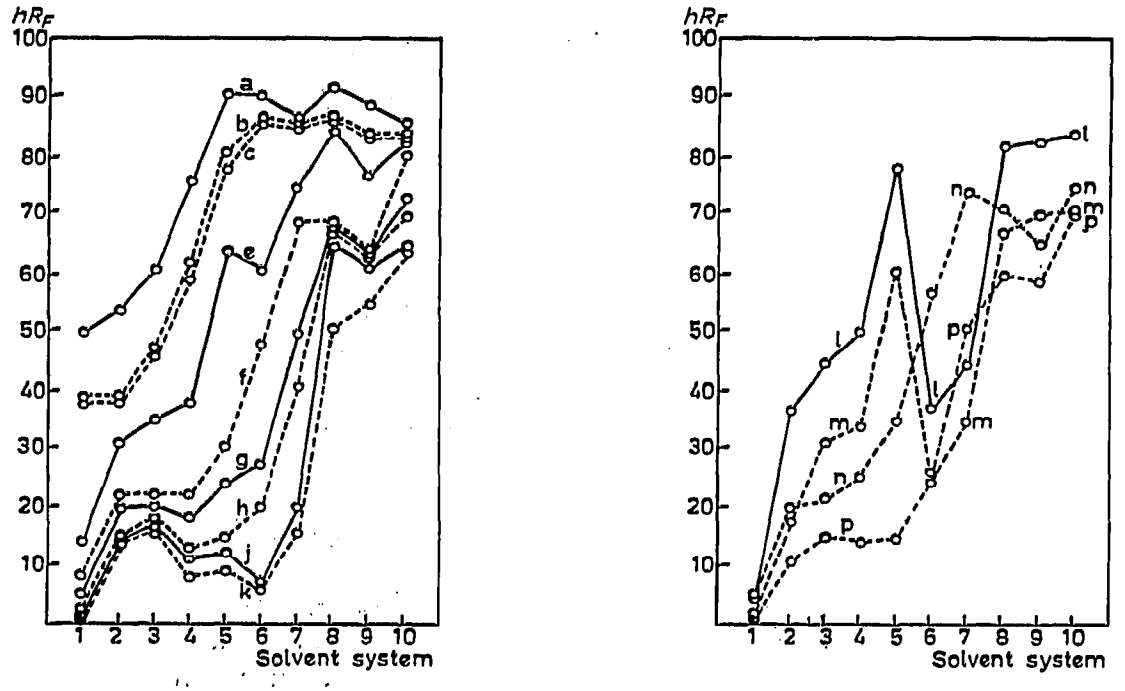


Fig. 3. hR_F values of closed E ring alkaloids (III, C(19)-CH_3 α): (a) tetrahydroalstonine (R = H, *allo*); (b) aricine (R = 10-OCH_3, *allo*); (c) reserpinine (R = 11-OCH_3, *allo*); (e) ajmalicine (R = H, *normal*); (f) tetraphylline (R = 11-OCH_3, *normal*); (g) akuammigine (R = H, *epiallo*); (h) isoreserpinine (R = 11-OCH_3, *epiallo*); (j) 3-isoajmalicine (R = H, *pseudo*); (k) mitrajavine (R = 9-OCH_3, *pseudo*).——— unsubstituted indole, – – – methoxy substituted indole.

Fig. 4. hR_F values of closed E ring alkaloids (III, C(19)-CH_3 β): (l) rauniticine (R = H, *allo*); (m) raunitidine (R = 11-OCH_3, *allo*); (n) raumitorine (R = 10-OCH_3, *normal*); (p) isoraunitidine (R = 11-OCH_3, *epiallo*). ——— unsubstituted indole, – – – methoxy substituted indole.

lower hR_F values than tetraphylline (f, III, R = 11-OCH_3, *normal*) Isoajmalicine (j, III, R = H, *pseudo*) has hR_F values higher than the corresponding 9-methoxy substituted alkaloid, mitrajavine (k, III, R = 9-OCH_3, *pseudo*) and lower hR_F values than isoreserpinine (h, III, R = 11-OCH_3, *epiallo*). Thus when the nine closed E ring alkaloids with C(19)-CH_3 α configuration are arranged in order of decreasing hR_F value the sequence is *allo*, *normal*, *epiallo* and *pseudo*, a methoxy substituted alkaloid having lower hR_F values than the corresponding unsubstituted alkaloid.

(*b*) *C(19)-CH₃ β configuration.* The behaviour, in the ten TLC systems, of four closed E ring alkaloids with C(19)-CH_3 β configurations is illustrated in Fig. 4. In systems Nos. 3, 4, 5 and 9 the sequence in order of decreasing hR_F value is *allo*, *normal* and *epiallo* but this is not so in the other systems. Rauniticine (l, III, R = H, *allo*) has slightly higher hR_F values than the corresponding 11-methoxy substituted alkaloid, raunitidine (m, III, R = 11-OCH_3, *allo*), both alkaloids showing a similar pattern of behaviour by having markedly low hR_F values in systems Nos. 6 and 7 in which silica gel is the adsorbent. In these two systems the *normal* alkaloid raumitorine (n, III, R = 10-OCH_3, *normal*) would be expected to have slightly lower hR_F values than raunitidine (m), the effect of a 10-methoxy substituent rather than an 11-methoxy substituent being to slightly increase hR_F values, though this difference would be smaller than the change in configuration from *allo* to *normal*. In fact the *normal* alkaloid raumitorine (n) has hR_F values higher than the *allo* alkaloid rauniti-

dine (m) and also higher than the unsubstituted *allo* alkaloid, rauniticine (l). In E *seco* alkaloids and closed E ring alkaloids with C(19)-CH_3 α a change in configuration at C(3) from α to β results in much lower hR_F values, but Fig. 4 shows that the *allo* alkaloid raunitidine (m) with a C(19)-CH_3 β configuration has hR_F values slightly lower than the corresponding *epiallo* alkaloid isoraunitidine (p, III, R = 11-OCH_3, *epiallo*) in systems Nos. 6 and 7.

When the hR_F values of the *allo* alkaloids with C(19)-CH_3 β configurations, raunticine (l) and rauntidine (m) are compared with the corresponding *allo* alkaloids which differ only in having C(19)-CH_3 α configurations, tetrahydroalstonine (a) and reserpinine (c), it can be seen that the effect of the C(19)-CH_3 β configuration is to lower hR_F values (Fig. 5). This behaviour is particularly noticeable in systems Nos. 1, 6 and 7 in which silica gel is the adsorbent. However this behaviour is not paralleled in the *normal* and *epiallo* alkaloids examined (Fig. 6), raumitorine (n, III, R = 10-OCH_3, C(19)-CH_3 β, *normal*) having similar hR_F values to tetraphylline (f, III, R = 11-OCH_3, C(19)-CH_3 α, *normal*) whilst isoraunitidine (p, III, 11-OCH_3, C(19)-CH_3 β, *epiallo*) and isoreserpinine (h, III, R = 11-OCH_3, *epiallo*) have similar hR_F values, the *normal* alkaloids having higher hR_F values than the *epiallo* alkaloids.

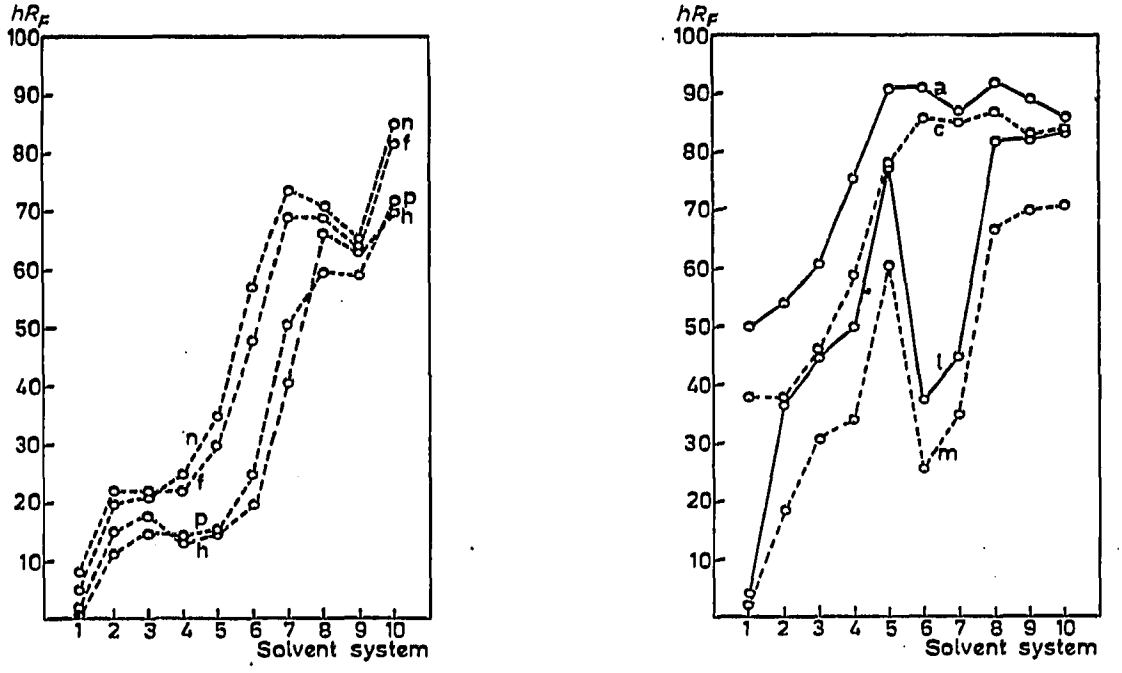


Fig. 5. hR_F values of *allo* closed E ring alkaloids (III): (a) tetrahydroalstonine (R = H, C(19)-CH_3 α); (c) reserpinine (R = 11-OCH_3, C(19)-CH_3 α); (l) rauniticine (R = H, C(19)-CH_3 β); (m) raunitidine (R = 11-OCH_3, C(19)-CH_3 β). ——— unsubstituted indole, – – – methoxy substituted indole.

Fig. 6. hR_F values of *normal* and *epiallo* closed E ring alkaloids (III): (n) raumitorine (R = 10-OCH_3, *normal*, C(19)-CH_3 β); (f) tetraphylline (R = 11-OCH_3, *normal* C(19)-CH_3 α); (p) isoraunitidine (R = 11-OCH_3, *epiallo*, C(19)-CH_3 β); (h) isoreserpinine (R = 11-OCH_3 *epiallo*, C(19)-CH_3 α). ——— unsubstituted indole, – – – methoxy substituted indole.

(*c*) *Dimethoxy substituted alkaloids.* Four dimethoxy substituted closed E ring alkaloids were examined on the ten TLC systems (Fig. 7). With the exception of minor differences in systems Nos. 3 and 5 these alkaloids can be arranged in order of

decreasing hR_F values as isoreserpiline (d, III, R = 10, 11-di-OCH_3, C(19)-CH_3 α, *allo*), rauvanine (o, III, R = 10, 11-di-OCH_3, C(19)-CH_3 β, *normal*), reserpiline (i, III, R = 10, 11-di-OCH_3, C(19)-CH_3 α, *epiallo*), epi-3-rauvanine (q, III, R = 10, 11-di-OCH_3, C(19)-CH_3 β, *pseudo*). Therefore the sequence in order of decreasing hR_F value is *allo*, *normal*, *epiallo* and *pseudo* even though the *allo* and *epiallo* alkaloids have C(19)-CH_3 α configuration and the *normal* and *pseudo* alkaloids have C(19)-CH_3 β configuration.

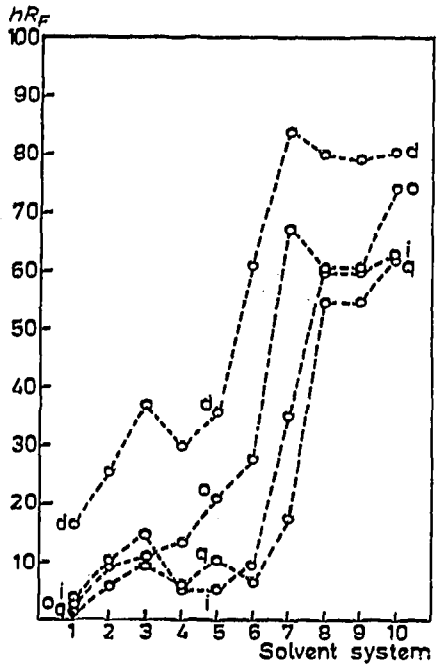


Fig. 7. hR_F values of 10, 11-dimethoxy substituted closed E ring alkaloids (III): (d) isoreserpiline (*allo*, C(19)-CH_3 α); (o) rauvanine (*normal*, C(19)-CH_3 β); (i) reserpiline (*epiallo*, C(19)-CH_3 α); (q) epi-3-rauvanine (*pseudo*, C(19)-CH_3 β).

An explanation of the fact that the two alkaloids having closed E rings C(19)-CH_3 β, *allo* configurations (rauniticine and raunitidine) behave abnormally with some TLC systems may be obtained by considering the nature of the chromatographic processes involved. Although it is possible that both partition and adsorption chromatography may take place at the same time on silica gel layers, since the plates are activated by heating at 105° for 30 min and stored, ready for use, over "tell-tale" silica gel, it is considered that the main process involved is that of adsorption.

The nature of the silica gel surface is illustrated in Fig. 8; showing that the silanol –OH groups project from the surface of the particles and are thus readily available for the adsorptive processes[21,22]. Indole, 4-, 5- and 6-methoxyindoles are adsorbed on the same TLC systems to a lesser extent than the heteroyohimbine alkaloids, so that adsorption of these alkaloids may be considered as due to:

(a) indole ring and its substituents and

(b) C, D, E rings and E ring substituents (II, III).

It is most likely that in (b) the main adsorption occurs by hydrogen bond formation between N(4) lone pair of electrons and the silanol –OH groups projecting from the surface of the silica gel particles[21–28],

i.e., —N: - - - - - H-O-Si—

When diethylamine is incorporated into the solvent system for silica gel plates (compare systems Nos. 1 and 10) the alkaloids tend to have higher hR_F values than when no diethylamine is present; this can be explained by the competition for hydrogen bond formation between diethylamine and the alkaloids for the silanol –OH groups.

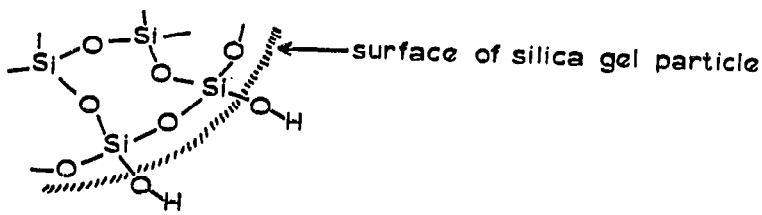
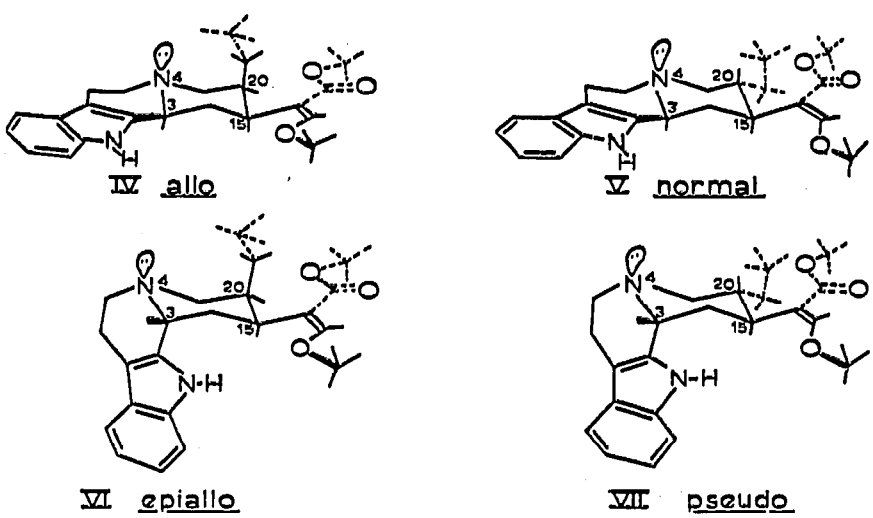
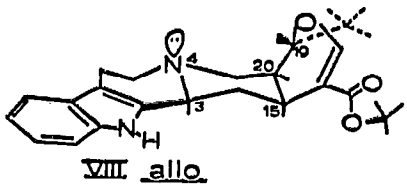


Fig. 8. Silica gel surface.

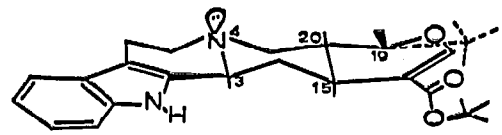


The N(4) lone pair of electrons of the alkaloids must be in a position for hydrogen bonding to take place with the silanol –OH groups and this will depend not only on configurational differences but on the preferred conformation for each configuration. The preferred conformation for the *allo*, *normal*, *epiallo* and *pseudo* configurations of the E *seco* alkaloids are shown as IV, V, VI and VII[3]. The *allo* (IV) and *normal* (V) configurations are more planar than the *epiallo* (VI) and *pseudo* (VII) configurations, the lone pair of electrons of N(4) being more accessible for hydrogen bond formation with the silanol –OH groups in the *epiallo* and *pseudo* configurations where N(4) is situated at a corner of the molecule whereas in the *allo* and *normal* configurations N(4) is centrally positioned in the more planar molecules. This would account for the fact that the *epiallo* and *pseudo* compounds are more strongly adsorbed than the *allo* and *normal* compounds. The C(20) ethyl group is closer to the N(4) lone pair electrons in the *allo* and *epiallo* configurations than in the *normal* and *pseudo* configurations hence hydrogen bonding would be easier in the latter two configurations. These considerations would account for the fact that the E *seco* alkaloids are

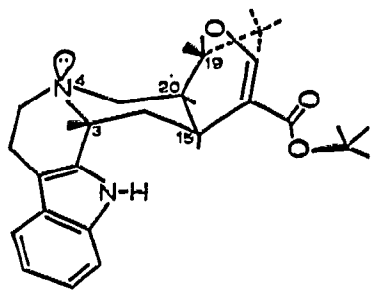
more strongly adsorbed (*i.e.*, decrease in hR_F values) in the sequence *allo*, *normal*, *epiallo* and *pseudo*.



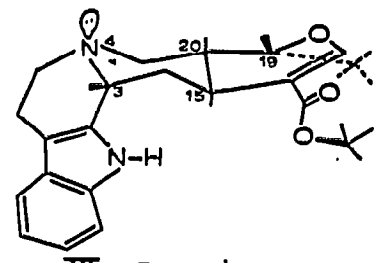
VIII allo



IX normal

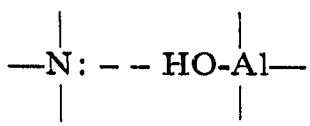


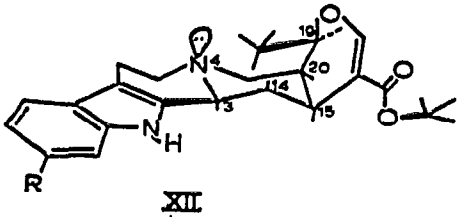
X epiallo



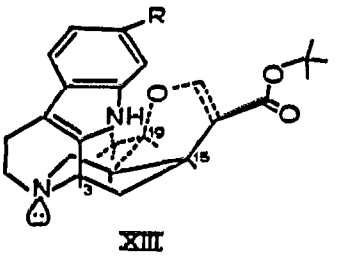
XI pseudo

The same arguments can be applied to the C(19)-CH_3 α closed E ring alkaloids, the preferred conformations for the *allo*, *normal*, *epiallo* and *pseudo* configurations being VIII, IX, X and XI respectively[15–17,29]. The only difference in this case being that the E ring lies closer to N(4) lone pair of electrons in the *allo* and *epiallo* configurations than in the *normal* and *pseudo* configurations, hence hydrogen bonding to the silanol –OH groups would be more difficult in the sequence *allo*, *normal*, *epiallo* and *pseudo*. These arguments can also be applied to the C(19)-CH_3 β closed E ring alkaloids, but there are, however, two apparent exceptions, *i.e.* the *allo* alkaloids, rauniticine (l) and raunitidine (m). In the preferred conformation for these two alkaloids, XII (raunticine, R = H; raunitidine, R = $-OCH_3$) assigned on the basis of I.R. and N.M.R. spectral data, p*Ka* values and rate of methiodide formation[17,29] the lone pair of electrons on N(4) are in close proximity to the C(19) methyl groups so that hydrogen bond formation with silanol –OH groups would be hindered. Changes in this conformation, by nitrogen inversion, to that shown in XIII have been reported under acid equilibrating conditions thus releasing the molecule from the steric crowding of the axial C(19) methyl group on the N(4) lone pair electrons and the C(14) β proton[29], and also during methiodide formation[17]. If during TLC on silica gel, rauniticine and raunitidine underwent a conformational change from XII to XIII, the N(4) lone pair electrons would be situated in such a position as to facilitate hydrogen bonding to the silanol –OH groups, thus explaining the extremely low hR_F values in silica gel systems Nos. 1, 6 and 7. Rauniticine and raunitidine also have low hR_F values in alumina systems Nos. 2–5, 8 and 9 when compared with the corresponding C(19)-CH_3 α alkaloids (Fig. 5) and it is possible that a conformational change also occurs on alumina since the surface of basic alumina may be considered as being similar to that of silica gel by having free projecting hydroxyl groups. Thus hydrogen bonding may also occur between the N(4) lone pair of electrons and the alumina –OH group.





XII



XIII

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SUMMARY

Indole, 4-, 5- and 6-methoxyindoles have been examined on TLC with twenty seven heteroyohimbine alkaloids. The results show that methoxy substituents lower hR_F values, that E *seco* alkaloids with C(20) vinyl groups have slightly higher hR_F values than the corresponding alkaloids with C(20) ethyl groups and that E *seco* and closed E ring alkaloids can be arranged in order of decreasing hR_F value as *allo*, *normal*, *epiallo* and *pseudo* with the exception of *allo* closed E ring alkaloids with a C(19)-CH_3 β configuration. The difference in adsorption has been explained in terms of hydrogen bonding between the N(4) lone pair electrons and the silanol –OH or alumina –OH groups whilst the exceptional TLC of two alkaloids has been accounted for by a change in their conformation, when undergoing adsorption.

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