# THE EFFECT OF METHOXY SUBSTITUTION AND CONFIGURATION ON THE THIN-LAYER CHROMATOGRAPHIC BEHAVIOUR OF SOME CLOSED E RING OXINDOLE ALKALOIDS

E. J. SHELLARD, J. D. PHILLIPSON AND D. GUPTA

*Pharmacognosy Research Laboratories, Department of Pharmacy, Chelsea College of Science and Technology, (University of London), Manresa Road, London, S.W. 3 (Great Britain)*

(Received September 21st, 1967)

PHILLIPSON AND SHELLARD[1] have compared the TLC behaviour of 12 E *seco* oxindole alkaloids of *allo* and *normal* configuration and have shown that A and B oxindole alkaloids are readily separated. The TLC behaviour of oxindole, hydroxy and methoxy oxindoles and indolizidine was also examined because these compounds correspond to the A, B, C and D rings of the alkaloids. The separations obtained between the alkaloids were related to their substitution and configurational differences, the differing adsorptions being explained in terms of oxindole carbonyl and tertiary nitrogen availability for hydrogen bond formation with adsorbent hydroxyl groups. SHAMMA *et al.*[2] have shown that *anti* oxindole alkaloids (*i.e.* N(4) and lactam carbonyl on opposite sides of the molecule) are less adsorbed on silica gel than the corresponding *syn* oxindole alkaloids (*i.e.* N(4) and lactam carbonyl on the same side of the molecule), but they did not compare the behaviour of different configurational types of *syn* and *anti* alkaloids. The TLC behaviour of two closed E ring alkaloids of known configuration, mitraphylline and isomitraphylline, has previously been described[3] and because speciophylline behaved like mitraphylline it was suggested that these two alkaloids might have the same configuration at spiro carbon C(7), *i.e.* speciophylline was an oxindole B alkaloid though it is known to be an oxindole A alkaloid[4]. This publication discusses the behaviour of speciophylline and relates the TLC behaviour of 17 other closed E ring oxindole alkaloids to their stereochemistry and methoxy substitution.

## METHODS

The details of plate preparation and development of the chromatograms has previously been described[3]. The following thin layer systems were used:

1. Alumina; cyclohexane–chloroform (3:7)
2. Alumina; cyclohexane–chloroform–diethylamine (3:7:0.005)
3. Alumina; chloroform
4. Alumina; ether–ethanol (95:5)
5. Alumina; chloroform–diethylamine (9:1)
6. Silica gel; benzene–ethyl acetate (7:2)
7. Silica gel; ether
8. Silica gel; ether–diethylamine (9:1)
9. Silica gel; chloroform–acetone (5:4)
10. Silica gel; ether–ethanol (95:5).

## RESULTS

The results of the separations are shown in Figs. 1–3, the $hR_F$ values given are the average of six separate determinations except for isocarapanaubine, rauvoxinine and the majdines, where only two determinations could be made.

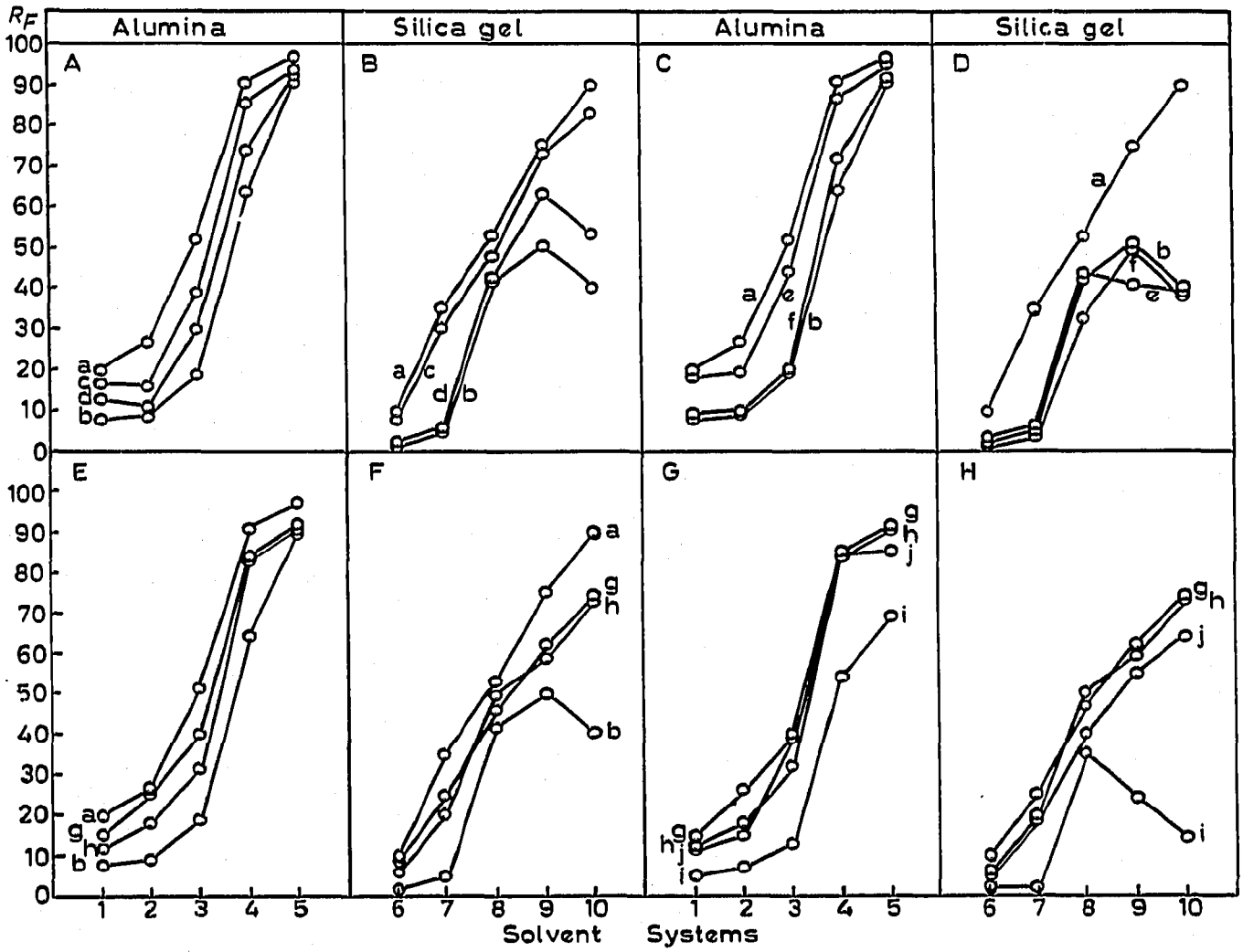
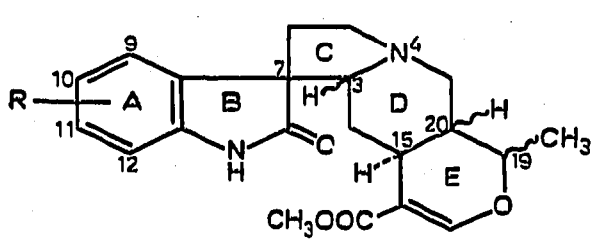



Fig. 1. $hR_F$ values of isomitraphylline (a), mitraphylline (b), uncarine A (c), uncarine B (d), javaphylline (e), isojavaphylline (f), isopteropodine (g), pteropodine (h), speciophylline (i) and uncarine F (j).

## DISCUSSION OF ALKALOIDAL STRUCTURE




I

There are sixteen theoretically possible unsubstituted closed E ring oxindole

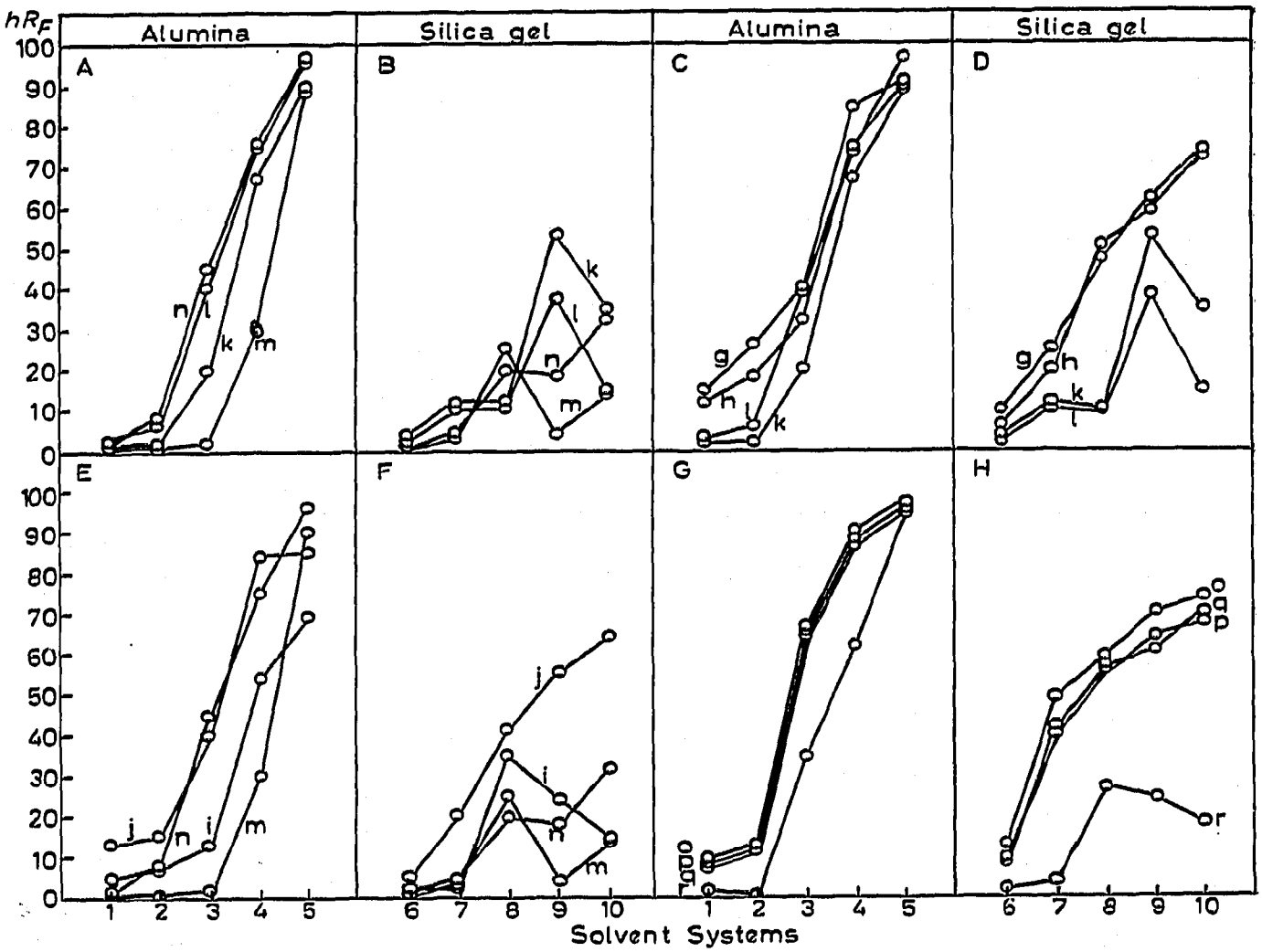



Fig. 2. $hR_F$ values of isopteropodine (g), pteropodine (h), speciophylline (i), uncarine F (j), isocarapanaubine (k), carapanaubine (l), rauvoxinine (m), rauvoxine (n), majdine 1 (o), majdine 2 (p), majdine 3 (q), and majdine 4 (r).

alkaloids[5] of the mitraphylline type (i, R = H)[2]. Configurational differences at C(3) and C(20) give rise to four possible isomers classified as:

*allo* C(3)–H$\alpha$, C(20)–H$\alpha$; *epiallo* C(3)–H$\beta$, C(20)–H$\alpha$;
*normal* C(3)–H$\alpha$, C(20)–H$\beta$; *pseudo* C(3)–H$\beta$, C(20)–H$\beta$.

Each one of these configurational types may differ in having an $\alpha$ or $\beta$ configuration of C(19)–$CH_3$ making eight theoretically possible isomers each of which may exist as an oxindole A or oxindole B type by a change of configuration at spiro carbon C(7).

The alkaloids examined are listed in Table I with their substitution and configurational differences. The term *syn* is used to describe alkaloids with oxindole carbonyl and N(4) on the same side of the molecule and *anti* when these two are on opposite sides of the molecule.

*The TLC behaviour of normal unsubstituted alkaloids with C(19)-Me$\alpha$ or -$\beta$ configurations*

These alkaloids can be arranged in order of decreasing $hR_F$ values on alumina

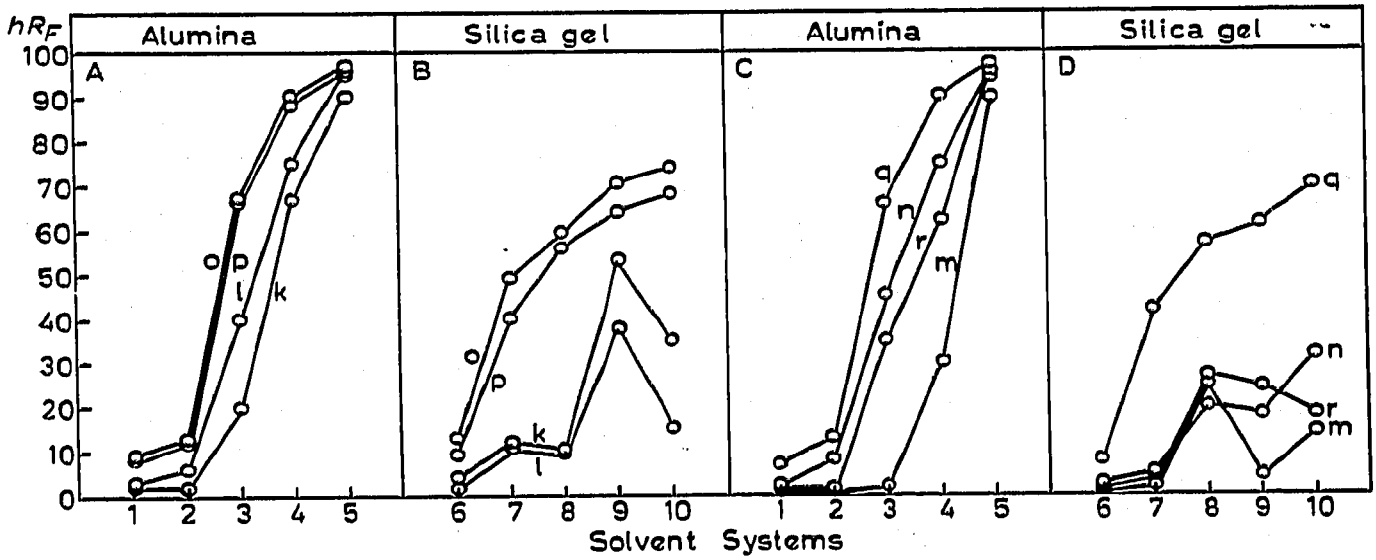



Fig. 3. $hR_F$ values of isocarapanaubine (k), carapanaubine (l), rauvoxinine (m), rauvoxine (n), majdine 1 (o), majdine 2 (p), majdine 3 (q), and majdine 4 (r).

TABLE I

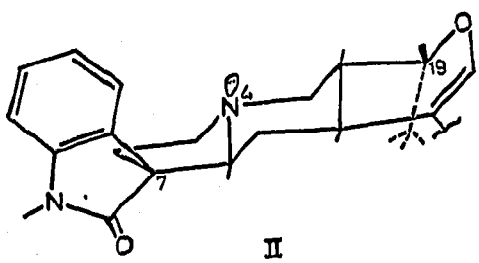
CONFIGURATIONS OF CLOSED E RING OXINDOLE ALKALOIDS (I)

| *Alkaloid** | *Type* | *C(7)* | *C(19)–$CH_3$* | *R* | *Oxindole (CO/$N_4$)* | *Reference* |
|---|---|---|---|---|---|---|
| (a) Isomitraphylline | *normal* | A | α | –H | *anti* | 6 |
| (b) Mitraphylline | *normal* | B | α | –H | *syn* | 6 |
| (c) Uncarine A (isoformosanine) | *normal* | A | β | –H | *anti* | 2<br>2 |
| (d) Uncarine B (formosanine) | *normal* | B | β | –H | *syn* | 2<br>2 |
| (e) Javaphylline | *normal* | A | α | 9-$OCH_3$ | *anti* | 7a, b |
| (f) Isojavaphylline | *normal* | B | α | 9-$OCH_3$ | *syn* | 7a, b |
| (g) Isopteropodine (uncarine C) | *allo* | A | α | –H | *anti* | 2<br>8 |
| (h) Pteropodine (uncarine E) | *allo* | B | α | –H | *syn* | 2<br>8 |
| (i) Speciophylline (uncarine D) | *epiallo* | A | α | –H | *syn* | 8 |
| (j) Uncarine F | *epiallo* | B | α | –H | *anti* | 8 |
| (k) Isocarapanaubine | *allo* | A | α | 10,11-di$OCH_3$ | *anti* | — |
| (l) Carapanaubine | *allo* | B | α | 10,11-di$OCH_3$ | *syn* | 2 |
| (m) Rauvoxinine | *epiallo* | A | α | 10,11-di$OCH_3$ | *anti* | 2 |
| (n) Rauvoxine | *epiallo* | B | α | 10,11-di$OCH_3$ | *syn* | 2 |
| (o) Majdine 1 | — | — | — | 10,11-di$OCH_3$ | — | 10, 11 |
| (p) Majdine 2 | — | — | — | 10,11-di$OCH_3$ | — | 10, 11 |
| (q) Majdine 3 | — | — | — | 10,11-di$OCH_3$ | — | 10, 11 |
| (r) Majdine 4 | — | — | — | 10,11-di$OCH_3$ | — | 10, 11 |

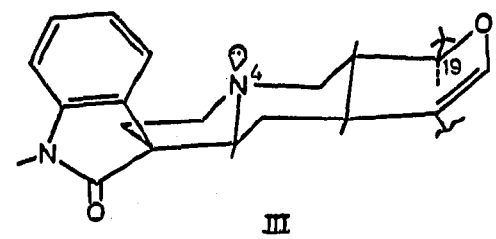
* Sources of alkaloids: (a) isomitraphylline; (b) mitraphylline, isolated from *Mitragyna speciosa*[9]; (c) uncarine A; (d) uncarine B supplied by Smith, Kline and French via Prof. A. H. BECKETT; (e) javaphylline isolated from *Mitragyna javanica*[7a]; (f) isojavaphylline by isomerisation of javaphylline[7b]; (g) isopteropodine; (h) pteropodine; (i) speciophylline; (j) uncarine F isolated from *Mitragyna parvifolia*[4]; (k) isocarapanaubine; (m) rauvoxinine by isomerisations of a micro quantity of carapanaubine and separation by preparative TLC; (l) carapanaubine; (n) rauvoxine supplied by Prof. J. POISSON; (p) majdine supplied by Dr. J. TROJANEK; (o) majdine 1; (p) majdine 2; (q) majdine 3; (r) majdine 4 by isomerisation of a microquantity of majdine and separation by preparative TLC.

and silica gel layers in the sequence of isomitraphylline (a, I, *normal*, A, C(19)–Me$\alpha$, R = H), uncarine A (c, I, *normal*, A, C(19)–Me$\beta$, R = H), uncarine B (d, I, *normal*, B, C(19)–Me$\beta$, R = H) and mitraphylline (b, *normal*, B, C(19)–Me$\alpha$, R = H) (Figs. 1A and B). It is clear that the *anti* alkaloids isomitraphylline and uncarine A have higher $hR_F$ values than the corresponding *syn* alkaloids mitraphylline and uncarine B. However, the change in configuration of the C(19)–Me in the A alkaloids from $\alpha$ (isomitraphylline) to $\beta$ (uncarine A) increases the adsorption on alumina and silica gel layers whilst in the B alkaloids the reverse is true, *i.e.* C(19)–Me$\alpha$ (mitraphylline) is more adsorbed than the C(19)–Me$\beta$ (uncarine B) alkaloid.

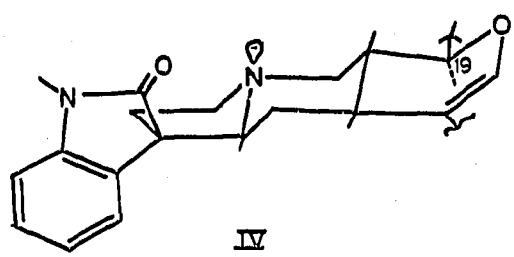
An explanation of this behaviour can be obtained by comparing the four isomers as made by Drieding models (II–V) (II, III, IV, V in sequence of decreasing $hR_F$ values).



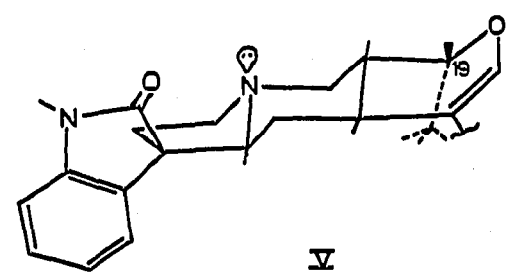

II




III




IV



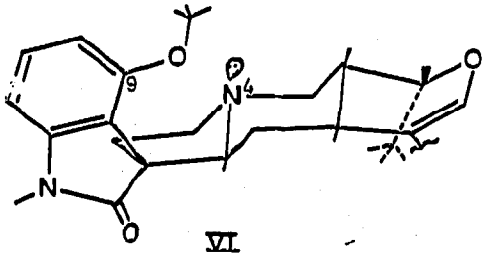

V

In the A *anti* alkaloids isomitraphylline (II) and uncarine A (III) adsorption can be considered mainly due to the oxindole carbonyl and not to the N(4) lone pair electrons which are hindered from binding with adsorbent hydroxyl groups due to the proximity of the benzene ring of the oxindole nucleus[1]. The C(19)·Me$\alpha$ configuration (II) has the axial methyl group on the same side of the molecule as the oxindole carbonyl tending to slightly hinder the oxindole carbonyl from acting as a site for adsorption and also tending to raise the D/E rings from the adsorbent surface. In the C(19)–Me$\beta$ oxindole A alkaloid (III) the C(19)–Me group is equatorial, lying in the plane of the D/E rings, and not at right angles to them, hence its position would not affect the availability of the oxindole carbonyl and would not tend to raise the D/E rings from the adsorbent surface.

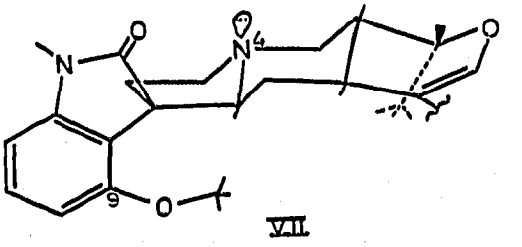
In the B *syn* alkaloids, uncarine B (IV) and mitraphylline (V), adsorption can be mainly considered due to oxindole carbonyl and N(4) lone pair electrons[1] and thus adsorption takes place from the opposite side of the molecule, reversing the effect of the C(19)-Me configuration when compared with the A alkaloids. The C(19)-Me$\alpha$ group is axial and away from both sites of adsorption but the C(19)–Me$\beta$ configuration slightly hinders the availability of N(4) by raising its level from the adsorbent surface.

*The TLC behaviour of normal unsubstituted alkaloids and 9-methoxy substituted alkaloids with C(19)-Meα configuration*

Fig. 1C shows that on alumina layers javaphylline (e, I, *normal* A, C(19)–Meα, R = C(9)–$OCH_3$) has $hR_F$ values slightly lower than the corresponding unsubstituted alkaloid, isomitraphylline, whilst isojavaphylline (f, I, *normal* B, C(19)–Meα, R = (C)9–$OCH_3$) has $hR_F$ values slightly higher than the corresponding unsubstituted alkaloid, mitraphylline. However, on silica gel layers (Fig. 1D) javaphylline behaves differently from isomitraphylline, having a behaviour pattern similar to that of mitraphylline and isojavaphylline.



VI



VII

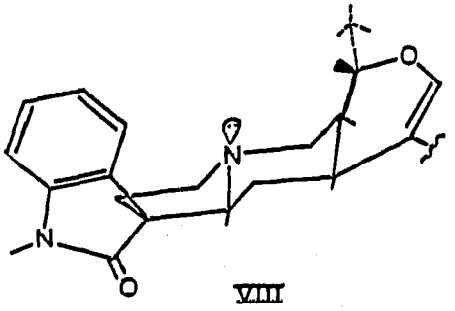
The presence of a 9-methoxy substituent in the A *anti* alkaloid javaphylline (VI) would not affect the availability of the oxindole carbonyl for adsorption and thus, cannot explain why javaphylline (VI) is slightly more adsorbed on alumina layers than isomitraphylline (II). In javaphylline the C(9)–$OCH_3$ is close to N(4) lone pair electrons and again this would not alter adsorption if N(4) is not involved because of hindrance by the oxindole benzene ring. Hence it is difficult to explain the differences of adsorption in these terms. Javaphylline (VI) is very strongly adsorbed on silica gel layers (Fig. 1D) and this behaviour is analogous to that of the corresponding E *seco* alkaloid, rhynchociline and its C(20) vinyl analogue, isospecionoxeine[1]. It is unlikely that N(4) inverts because resulting conformers would be too unstable; however it may be possible that the close proximity of C(9)–$OCH_3$ to N(4) enables adsorption to take place at N(4) instead of at the oxindole carbonyl though this would not explain the different behaviour on alumina. The fact that indolizidine is strongly adsorbed on silica gel layers rather than on alumina layers[1] indicates that in javaphylline N(4) is the most likely site of adsorption.

Isojavaphylline (VII), a B *syn* alkaloid, would be expected to have similar adsorption behaviour to mitraphylline (V) (Figs. 1C and D) since the C(9)–$OCH_3$ lies away from the sites of adsorption (N(4) and oxindole carbonyl).

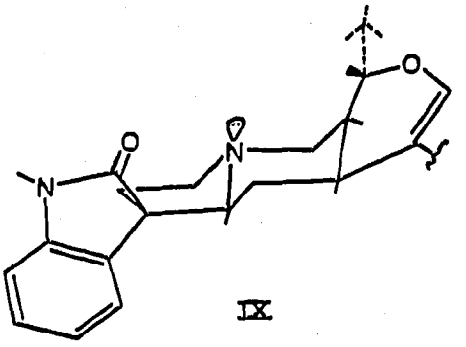
*The TLC behaviour of normal and allo unsubstituted alkaloids with C(19)-Meα configuration*

Figs. 1E and F show that the two *allo* alkaloids isopteropodine (g, I, *allo*, A, C(19)–Meα, R = H) and pteropodine (h, I, *allo*, B, C(19)–Meα, R = H) have $hR_F$ values, on alumina and silica gel layers, intermediate to those of the corresponding *normal* alkaloids, isomitraphylline and mitraphylline. If it is considered that adsorption of the two A *anti* alkaloids, isomitraphylline (II) and isopteropodine (VIII), takes place only at the oxindole carbonyl and not at N(4), then the difference in adsorption can be explained by reference to Dreiding models of the alkaloids. In isomitraphylline (II) the C/D/E rings lie in one plane and in order for the oxindole carbonyl to be available for bonding these three rings must be in contact with the adsorbent surface

whereas in isopteropodine (VIII) the E ring will curve away from the adsorbent surface so that the oxindole carbonyl would be less hindered from approaching adsorbent hydroxyl groups.



VIII



IX

Adsorption of the *syn* B alkaloids mainly takes place by oxindole carbonyl and N(4) and in the *allo* alkaloid pteropodine (IX) the position of the E ring will hinder the availability of N(4) when compared with mitraphylline (V). Thus it can be seen that whilst the *normal* A and B oxindole alkaloids are easily separated on alumina and silica gel layers the *allo* A and B alkaloids are not so readily separated and tend to have similar $hR_F$ values.

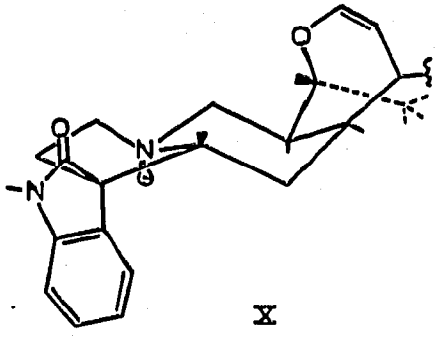
*The TLC behaviour of allo and epiallo unsubstituted alkaloids with C(19)-Meα configuration*

Figs. 1 G and H show that these alkaloids can be arranged in order of decreasing $hR_F$ values, on alumina and silica gel layers, in the sequence isopteropodine (g, I, *allo*, A, C(19)–Meα, R = H), pteropodine (h, I, *allo*, B, C(19)–Meα, R = H), uncarine F (j, I, *epiallo*, B, C(19)–Meα, R = H) and speciophylline (i, I, *epiallo*, A, C(19)–Meα, R = H)*.

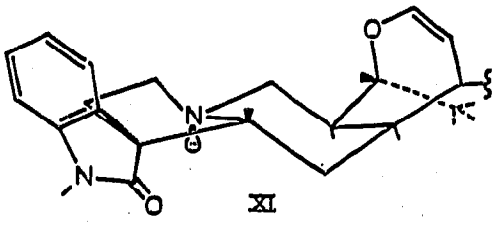
The *epiallo* alkaloid, uncarine F (X), forms a more stable conformation by inversion of N(4)[8b], becoming an *anti* alkaloid instead of a *syn*, and hence adsorption would be mainly due to the oxindole carbonyl and not to N(4). This would explain why uncarine F has similar $hR_F$ values on alumina and silica gel layers to the *allo* alkaloids, isopteropodine and pteropodine in which the oxindole carbonyl is mainly responsible for adsorption. The *epiallo* A alkaloid, speciophylline (XI), also forms a more stable conformation by inversion of N(4)[8b], becoming a *syn* instead of an *anti* alkaloid. The E ring in speciophylline curves away from the oxindole carbonyl and N(4) so that these sites are both readily available for adsorption. Hence speciophylline, although an oxindole A alkaloid, is similar to the *normal* B alkaloid mitraphylline (V) in that adsorption is due to oxindole carbonyl and N(4). On silica gel layers speciophylline is far more strongly adsorbed than uncarine F, isopteropodine and pteropodine in four systems but in system 8 (ether–diethylamine) speciophylline

* Uncarine D[8a] kindly supplied by Dr. S. R. JOHNS (through Prof. A. H. BECKETT) has identical $hR_F$ values in all systems used with speciophylline; pyridine isomerisation of speciophylline yielded two alkaloids, separated by preparative TLC, with identical $hR_F$ values in all systems to pteropodine and isopteropodine. This indicates that uncarine D is identical to speciophylline and this has been confirmed by comparison of I.R., NMR and CD spectra[4]. A comparison of papers published by SHAMMA *et al.*[2] and BEECHAM *et al.*[8b] indicates that uncarine C is identical to isopteropodine and that uncarine E is identical to pteropodine.

has $hR_F$ values higher than expected. This indicates that N(4) takes part in adsorption, the behaviour being similar to that of indolizidine[1].



X



XI

*The TLC behaviour of allo and epiallo 10,11-dimethoxy substituted alkaloids with C(19)–Meα configuration*

Fig. 2A shows that on alumina layers these alkaloids can be arranged in sequence of decreasing $hR_F$ value as rauvoxine (n, I, *epiallo*, B, C(19)–Meα, R = 10,11-diMeO), carapanaubine (l, I, *allo*, B, C(19)–Meα, R = 10,11-diMeO), isocarapanaubine (k, I, *allo*, A, C(19)–Meα, R = 10,11-diMeO) and rauvoxinine (m, I, *epiallo*, A, C(19)–Meα, R = 10,11-diMeO). The behaviour of rauvoxinine is similar to that of the corresponding unsubstituted alkaloid, speciophylline (XI), but although the other three alkaloids have similar $hR_F$ values the sequence in order of $hR_F$ is opposite to the sequence of the corresponding unsubstituted alkaloids. The presence of 10,11-dimethoxy substituents at the opposite side of the oxindole portion to the carbonyl does not hinder the accessibility of the oxindole carbonyl for adsorption to take place. It is not surprising that the *epiallo* B alkaloid is the least adsorbed because the E ring would tend to hinder the availability of the oxindole carbonyl but surprisingly this is not the case for the corresponding unsubstituted alkaloid (X). Figs. 2C and D show that the effect of dimethoxy substituents is to increase adsorption of *allo* alkaloids on alumina and silica gel layers. Since *allo* A adsorption can be considered mainly due to the oxindole carbonyl then it is possible that the 10-methoxy substituent, which has an inductive effect on the oxindole carbonyl, enables it to be more strongly bonded to adsorbent hydroxyl groups. However, the increase in adsorption due to the 10,11-dimethoxy substituents is greater than that expected due to induction of the oxindole carbonyl as previously shown when the adsorption of oxindole and 5-methoxy-oxindole are compared[1]. A further possibility is that adsorption occurs at the methoxy substituents so that there may be competition between them and the oxindole carbonyl as sites for adsorption. With *allo* B alkaloids adsorption is due to oxindole carbonyl and partly hindered N(4) so that any competition for adsorption is between the dimethoxy groups and the two centres, oxindole carbonyl and N(4), at the opposite side of the molecule; with the result that the presence of two methoxy groups affects the adsorption of the *allo* B to a greater extent than the *allo* A, reversing their order of adsorption when compared with the corresponding unsubstituted alkaloids.

On silica gel layers there is no clear behaviour sequence for the four dimethoxy substituted alkaloids (Fig. 2). Isocarapanaubine (*allo* A) has higher $hR_F$ values than carapanaubine (*allo* B), reversing their sequence on alumina, but the two do have a similar behaviour pattern and are more strongly adsorbed than the corresponding

unsubstituted alkaloids (Fig. 2D). In four of the five silica gel systems, rauvoxinine (m, *epiallo* A) has lower $hR_F$ values than carapanaubine and isocarapanaubine whereas rauvoxine (n, *epiallo* B) has lower $hR_F$ values than carapanaubine and isocarapanaubine in three systems, higher $hR_F$ value in one system and an intermediate $hR_F$ value in another system (Fig. 2B). The fact that rauvoxine and rauvoxinine both have higher $hR_F$ values than carapanaubine and isocarapanaubine in system 8 (silica gel; ether–diethylamine, 9:1) indicates that N(4) takes part in adsorption because the behaviour is similar to indolizidine[1]. The adsorption of rauvoxinine (m, *epiallo* A) would, therefore, be similar to speciophylline (XI), the corresponding alkaloid, in that the oxindole carbonyl and N(4) are involved, but the adsorption of rauvoxine (n, *epiallo* B) would be dissimilar to that of uncarine F (X) where only oxindole carbonyl is presumed to be involved. The presence of two methoxy substituents on the same side of the molecule to N(4) but on the opposite side to the oxindole carbonyl may explain the anomalous behaviour of rauvoxine on silica gel layers (Figs. 2E and F).

*TLC behaviour of majdine isomers*

By isomerisation of microquantities of majdine using pyridine and also acetic acid, four isomers were produced which were separated by preparative TLC. These four isomers were numbered 1, 2, 3 and 4 in order of decreasing $hR_F$ values on alumina and silica gel systems (Fig. 2, G and H). Original majdine corresponds to majdine 2 on all systems. The fact that four isomers are produced indicates that majdine belongs to the *allo/epiallo* series. Since it has been reported that majdine is a 10,11-dimethoxy substituted closed E ring oxindole alkaloid[11] though with unspecified configurations at C(3), C(19), C(20) and C(7), as these four isomers are different from isocarapanaubine, carapanaubine, rauvoxine and rauvoxinine which have the C(19)–Me$\alpha$ configuration (Figs. 3A, B, C and D) it would appear that they must possess C(19)–Me$\beta$ configuration, assuming the universal configuration C(15)–H$\alpha$.

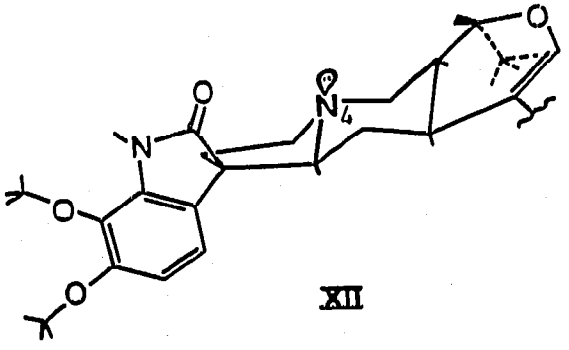
Three of the majdine isomers have similar $hR_F$ values on alumina and silica gel layers whilst the fourth, majdine 4, is more strongly adsorbed (Figs. 2G and H) and this behaviour is similar to that of the *allo* and *epiallo* unsubstituted alkaloids with C(19)–Me$\alpha$ configuration. As shown in Figs. 3A and B, majdine 1 and 2 have higher $hR_F$ values on alumina and silica gel layers than the two disubstituted C(15)–Me$\alpha$ alkaloids isocarapanaubine (*allo* A) and carapanaubine (*allo* B) while majdine 3 and majdine 4 have higher $hR_F$ values than the two disubstituted C(19)–Me$\alpha$ alkaloids rauvoxine (*epiallo* B) and rauvoxinine (*epiallo* A) (Figs. 3C and D). Hence in all four majdine isomers it would appear that the effect of the C(19)–Me$\beta$ configuration is to decrease adsorption though it is difficult to understand why this should be so with all four isomers.

In the *allo* B majdine it is possible that the C(19)–Me$\beta$ could hinder the availability of N(4) so that an alkaloid with a C(19)–Me$\beta$ configuration would be less strongly adsorbed than the corresponding alkaloid with a C(19)–Me$\alpha$ configuration. However, in the *allo* A majdine, although the C(19)–Me$\beta$ could affect the availability of N(4), it is considered that N(4) takes no part in the adsorption of the substance so that it is difficult to see why this change in configuration would affect adsorption since the C(19)-Me of the *allo* A compound does not affect the availability of the oxindole carbonyl. A possible explanation is that a methoxy group at a position

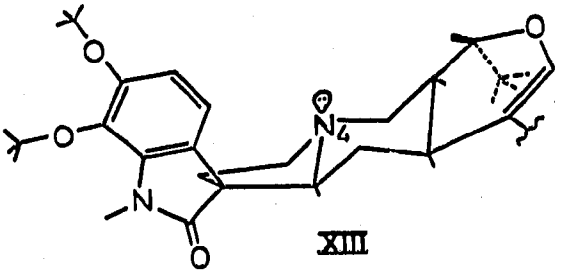
other than C(10) would have a greatly reduced inductive effect on the oxindole carbonyl.

It is also difficult to understand why a change in configuration of C(19)–Me from $\alpha$ to $\beta$ should result in a decrease in adsorption of the *epiallo* $\beta$ majdine where again adsorption can be considered as mainly due to the oxindole carbonyl and not the N(4). The decrease in adsorption can, however, be explained if a methoxy group is present at C(12) and not C(10).

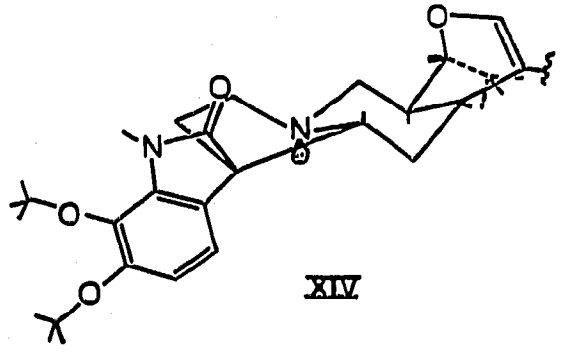
The C(19)–Me$\beta$ configuration in the *epiallo* A majdine could offer some hindrance to the availability of N(4) and thus explain why majdine 4 has higher $hR_F$ values than rauvoxinine (Figs. 3C and D) but this can also be accounted for by the presence of $-OCH_3$ at C(12). The strong adsorption of the *epiallo* A compounds is considered due to joint adsorption by N(4) and the oxindole carbonyl so that the latter would undoubtedly be affected by the presence of C(12)–$OCH_3$.



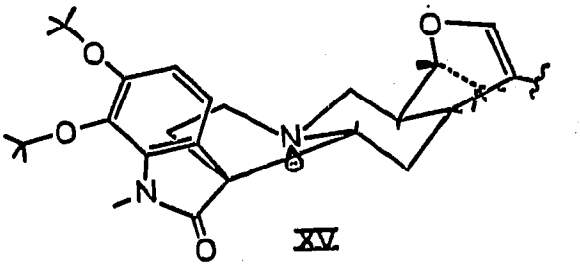
XII



XIII



XIV



XV

Since the behaviour on TLC of the majdine isomers is so very similar to that of the *allo/epiallo* unsubstituted alkaloids having C(19)–Me$\alpha$ configuration and as the difference in behaviour between the majdines and the 10,11-disubstituted *allo/epiallo* alkaloids having C(19)–Me$\alpha$ configuration is not explained satisfactorily by merely changing the C(19)–Me configuration to $\beta$, though it can be explained by considering substitution in ring A at C(12) it is more than probable, that, in spite of the previously reported claim[11], majdine is a 11,12-dimethoxy substituted closed E ring oxindole alkaloid, *allo* A, with C(19)–Me$\alpha$ configuration. (This assumes the di-substitution to be *ortho*). Thus majdine 1 (*allo* B), majdine 2 (*allo* A), majdine 3 (*epiallo* B) and majdine 4 (*epiallo* A) may be represented as XII, XIII, XIV and XV respectively, so that Table I could be corrected as follows:

| | *Type* | *C(7)* | *C(19)–CH₃* | *R* | *CO/N(4)* |
|---|---|---|---|---|---|
| (o) Majdine 1 | *allo* | A | α | 11,12-diOCH₃ | *syn* |
| (p) Majdine 2 (majdine[10,11]) | *allo* | B | α | 11,12-diOCH₃ | *anti* |
| (q) Majdine 3 | *epiallo* | B | α | 11,12-diOCH₃ | *anti* |
| (r) Majdine 4 | *epiallo* | A | α | 11,12-diOCH₃ | *syn* |

It will be interesting to see whether these conclusions based on the TLC behaviour of the alkaloids are confirmed by more sophisticated studies using I.R., NMR, CD etc.

ACKNOWLEDGEMENTS

We would like to thank the following for generously supplying samples: Smith, Kline and French Laboratories for uncarines A and B (through Prof. A. H. BECKETT), Prof. J. POISSON for carapanaubine and rauvoxine and Dr. J. TROJANEK for majdine.

We are grateful to Prof. W. H. HUNTER for helpful discussions and to Mr. R. BROWN for the diagrams.

SUMMARY

The TLC behaviour of eighteen closed E ring oxindole alkaloids on alumina and silica gel layers is described and the separations are related to configuration. The differing adsorptions are explained in terms of oxindole carbonyl and N(4) availability for hydrogen bond formation with adsorbent hydroxyl groups. Oxindole A alkaloids of *normal* configuration are less adsorbed than the corresponding B alkaloids from which they are readily separated whilst *allo* A and B alkaloids tend to be more difficult to separate. Because of nitrogen inversion to form a more stable conformer the *epiallo* A alkaloid, speciophylline, has a behaviour pattern similar to the *normal* B alkaloid mitraphylline and is more strongly adsorbed than the corresponding *epiallo* B alkaloid. The TLC behaviour of four majdine isomers of unknown stereochemistry is discussed.

REFERENCES

1 J. D. PHILLIPSON AND E. J. SHELLARD, *J. Chromatog.*, 32 (1968) 692.
2 M. SHAMMA, R. J. SHINE, I. KOMPIS, T. STICZAY, F. MORSINGH, J. POISSON AND J. L. POUSSET, *J. Am. Chem. Soc.*, 89 (1967) 1739, and references therein.
3 J. D. PHILLIPSON AND E. J. SHELLARD, *J. Chromatog.*, 24 (1966) 84.
4 E. J. SHELLARD, J. D. PHILLIPSON AND D. GUPTA, *Planta Med.*, 16 (1968) in press.
5 J. E. SAXTON, in R. H. F. MANSKE (Editor), *The Alkaloids*, Vol. VIII, Academic Press, New York, 1965, p. 59*ff*.
6 N. FINCH AND W. I. TAYLOR, *J. Am. Chem. Soc.*, 84 (1962) 1318 and 3871.
7 (a) E. J. SHELLARD, A. H. BECKETT, P. TANTIVATANA, J. D. PHILLIPSON AND C. M. LEE, *Planta Med.*, 15 (1967) 245; (b) A. H. BECKETT, W. F. TRAGER, C. M. LEE AND J. D. PHILLIPSON, unpublished.
8 (a) S. R. JOHNS AND J. A. LAMBERTON, *Tetrahedron Letters*, No. 40 (1966) 4883; (b) A. F. BEECHAM, N. K. HART, S. R. JOHNS AND J. A. LAMBERTON, *Tetrahedron Letters*, (1967) 991.
9 A. H. BECKETT, E. J. SHELLARD, J. D. PHILLIPSON AND C. M. LEE, *Planta Med.*, 14 (1966) 266.
10 J. L. KAUL AND J. TROJANEK, *Lloydia*, 29 (1966) 26.
11 N. ABDURAKHIMOVA, P. CH. YULDASHEV AND S. YU. YUNUSOV, *Khimis Prirodrych Sol.*, 1 (1965) 224.