THE CONNECTION BETWEEN THE IÓNIZATION CONSTANTS OF ALKALOIDS AND THEIR BASICITIES

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On performing a series of experiments on the polybuffer distribution of the alkaloids of V. erecta between chloroform and buffer solutions with decreasing pH values, we have found that there is the following sequence of passage of the basic alkaloids into the buffer solution which is repeated in all cases:

pH of Passage of the Alkaloids of V. erecta

Alkaloid	pH of passage into the buffer
Tombosine	5,5–6,0
Vincanidine	5.0–5,5
Akuammidine	4.5–5.0
Vincarine	3,5–4,5
Vincanine	3,0–3.5
Vincamine	2.0–3,0
Ervamine	10% H_2SO_4

It is clear that on passing from tombosine to ervamine the basicities of the alkaloids decrease [1]. In view of the fact that in an organic phase the alkaloids must be present in the form of free bases, and in a buffer solution in the form of salts, we assumed that the distribution of the alkaloids in the two phases should be governed by the ionization constants, since it is known [2] that, in the first place, precisely half the alkaloids are present in the salt form, when $pH = pK_a$; in the second place, 90% of the alkaloids are present in the form of the free bases, when $pH = pK_a + 1$; and, in the third place 90% of the alkaloids are in the salt form when $pH = pK_a - 1$. Consequently, we determined the pK_a values of the alkaloids of V. erecta potentiometrically by a literature method [3] (Table 1). In view of the fact that the free alkaloids are practically insoluble in water, we used a 20% solution of methanol in double-distilled water as the solvent. As follows from the literature information, in such cases the pK_a values of the amines decrease by about 10% [4].

Titration was performed with a 0.01 N solution of hydrochloric acid. The end of the titration was determined from the largest jump in potential in the relative $\Delta V = f(\Delta pH)$ [2].

It did not appear possible to establish the relationship between the pK_a value and the pH of transition from chloroform into buffer solutions. Assuming that the pH of transition into the buffer solution may depend on the pK_a value of the base in chloroform, we found the pK_a values of the alkaloids in chloroform. Titration was performed with a 0.01 N solution of hydrogen chloride in ethanol. The potentiometric titration curve showed a well-defined jump, and therefore it was easily possible to determine the end of the titration. The pK_a values were calculated by a literature method [3].

TABLE 1. Ionization Constants of the Alkaloids of V. erecta

Alkaloid	pK_a values	
	20% methanol	chloroform
Vincamine	6,62	5,81
Vincanine	7,79	5,72
Vincarine	6,91	5,73
Akuammidine	6,66	5,15
Vincanidine	6,84	5,91
Tombosine	7,54	6,30

As can be seen from Table 1, in chloroform a relative leveling-out of the pK_a values takes place. Thus, neither in water nor in chloroform are the pK_a values of the alkaloids connected with the pH range for the transition of the alkaloids from chloroform into a buffer solution.

Information on the main opium alkaloids, which is given in Table 2, confirms our conclusion that the pK_a values of the alkaloids cannot quantitatively describe the process of the distribution of the alkaloids in hetero-

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TABLE 2. Ionization Constants of Opium Alkaloids and the pH of Transition

Alkaloid	pK_a [7]	pH of transition [5, 6]
Morphine	7,87	6,0
Codeine	7,95	4,5
Thebaine	7,00	2,0
Papaverine	5,90	Do not pass over at pH = 1.0
Narcotine	6,18	

geneous systems of the organic solvent–buffer solutions type and, consequently, do not reflect the relative strengths of their basicity. For example, the difference between the pK_a values of morphine and thebaine $\Delta pK_a = 0.87$, while ΔpH for the transition process is 4 units; pK_a for codeine > pK_a for morphine, and the pH of the transition of morphine > pK_a for codeine, as also in the case of the indole alkaloids.

EXPERIMENTAL

Potentiometric Titration. Titration was performed on an LPM-60M pH-meter. Solutions of the substances under investigation in 20% ethanol in double-distilled water were prepared at concentrations of $1.2-8.0 \cdot 10^{-4}$ M and were titrated with 0.01 N hydrochloric acid solution (see Table 1). Solutions in chloroform with a concentration of $1 \cdot 10^{-2}$ M were titrated with a 0.01 N solution of hydrogen chloride in ethanol (see Table 1).

SUMMARY

1. The pK_a values of a number of indole alkaloids of Vinca erecta in aqueous ethanolic solution and in chloroform have been determined.

2. It has been shown that the pK_a value of an alkaloid in water or in chloroform is not connected with the pH of the transition from chloroform into a buffer solution.

3. It is impossible to estimate the basicity of an alkaloid from its pK_a value.

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