ALKALOIDS FROM *Eschscholtzia lobbii* GREENE*

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In addition to protopine allocryptopine, (−)-scoulerine, corytuberine and coptisine were isolated from *Eschscholtzia lobbii* GREENE, and small amounts of corydine, sanguinarine, chelirubine, chelerythrine, macarpine, berberine and corysamine were also detected.

The alkaloids of *Eschscholtzia lobbii* GREENE, from the section *Stenocraspedontae* FEDDE, were the subject of our studies several years ago[1]. Protopine was found as the main alkaloid in addition to a negligible amount of sanguinarine and coptisine, and traces of berberine. Now we used a larger amount of plant material from two collections (alkaloid content 0·061% or 0·046% of dry plant) for our study and we also tried to isolate and identify other minor alkaloids. After protopine we isolated a small amount of allocryptopine from the mother liquors and in the fraction of quaternary benzophenanthridines we proved the presence of chelirubine, chelerythrine and macarpine in addition to sanguinarine. In the fraction of hydrochlorides which are extractable with chloroform we found a small amount of corydine. The main component of the phenolic fraction was (−)-scoulerine, in addition to other unidentified bases. We isolated coptisine from the fraction of quaternary protoberberines in the form of a weakly soluble chloride and we detected small amounts of berberine and corysamine in the mother liquors. Further, corytuberine was also obtained, best by extraction of its hydriodide into chloroform[2].

Quaternary alkaloids were found in trace amounts only.

These results of the study of alkaloids from *E. lobbii* species are contribution to the biochemical characterization of the genus *Eschscholtzia* which is known as a taxonomically difficult group. According to different views of various botanists the *Eschscholtzia* genus comprizes either only two very plastic and polytypic main species with various oecotypes and cytotypes, or a large number of small species[3]. Fedde[4] mentions 123 species classified into two sections, *Eurycraspedonteae* and *Stenocraspedontae*. In spite of the small number of species the alkaloids of which have been studied so far, three biochemically different groups may already be differentiated

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within the *Eschscholtzia* genus. The species *E. californica* CHAM., *E. glauca* GREENE and *E. douglasii* (HOOK. et ARN.) WALP., belong to the first group all from the *Eurycraspedontae* section, characterized by the prevalence of pavine type alkaloids and a high content of quaternary alkaloids (see[1,5-8]). The second group consists of the species *E. cf. oregana* GREENE (section *Stenocraspedontae*), which displays a high content of quaternary alkaloid escholamine of the papaverine type as the major alkaloid component[1,9]. The species *E. lobbii* GREENE belongs to the third group, also from the *Stenocraspedontae* section, containing mainly protopine type alkaloids (also present in other species) and characterized by the occurrence of scoulerine and corytuberine, and especially by the fact that it is practically devoid of quaternary alkaloids.

EXPERIMENTAL

The melting points were determined both in capillaries and on a Kofler block, and they were not corrected. The mass spectrum was measured on an AEI — MS 902 mass spectrometer, the IR spectra (in KBr) on an Infrascan, Hilger and Watts instrument, and the UV spectra (in methanol) on a Unicam SP 500 spectrophotometer. For thin layer chromatography both silica gel G (Merck) with gypsum (5 : 1) was used in combination with the systems cyclohexane–diethylamine 9 : 1 (S_1), cyclohexane–chloroform–diethylamine 7 : 2 : 1 (S_2) and 4 : 5 : 1 (S_3), hexane–chloroform–methanol 5 : 4 : 1 (saturated with formamide, S_4), methanol–diethylamine 4 : 1 (S_5), 1-propanol–water–85% formic acid 7 : 2 : 1 (S_6), ethanol–water–25% ammonia 15 : 9 : 1 (S_7) and methanol–diethylamine 1 : 1 (S_8), and Silufol UV 254 (Kavalier) with the systems methanol–cyclohexane 1 : 1 (S_9), hexane–chloroform–methanol 5 : 4 : 6 (S_{10}), and methanol–diethylamine 1 : 1 (S_{11}). Paper chromatography was carried out in descending manner on Whatman paper No 1 with 1-butanol–acetic acid–water 10 : 1 : 3 (S_{12}). Detection of fluorescent spots was carried out under UV light, while other spots were detected with potassium iodoplatinate or Dragendorff's reagent.

Extraction and Isolation of Alkaloids

The plants were cultivated in the Experimental botanical garden, Medical Faculty, Brno, from the seeds of plants used in paper[1] and collected at the stage of flowering and unripe fruits at the end of June and beginning of July in 1967—1969 (sample I) and 1972 (sample II). The plants were dried at room temperature. Both samples were worked up separately (in further text the yields are mentioned from sample I or sample II). Dry, ground plants (sample I: 5·03 kg; sample II: 7·90 kg) were extracted with methanol, the extract was worked up in principle in the same manner as in paper[1], and the alkaloidal fractions were separated in the sequence *A*, *B*, *E* and *I* (sample I), or *A*, *B*, *I* and *E* (sample II).

The crude bases of fraction *A* were separated to fractions *AC*, AD_1 and AD_2 (see[10]). On crystallization of fraction *AC* from ether a small amount of protopine and scoulerine could be separated. The amorphous residue consisted mainly of substances of non-alkaloidal nature, after the separation of which 0·03 g of amorphous bases remained (sample I). In addition to a residue of protopine, allocryptopine and scoulerine a small amount of corydine could be detected in them (R_F 0·20 in S_1 and 0·53 in S_2, after detection with potassium iodoplatinate a green-blue spot appeared, identical with that of an authentic specimen), and two additional unidentified bases (R_F 0·58 and 0·68 in S_1, 0·76 and 0·82 in S_2). Protopine was obtained from fraction AD_1 by crystallization

from ether (total yield 1·84 g or 2·11 g; 0·037 or 0·027%), which melted at 207—208°C (chloroform–ethanol; capillary), and allocryptopine (0·08 g or 0·27 g; 0·0016 or 0·0034% respectively), m.p. 159—160°C (ethanol, capillary). The identity of both alkaloids was confirmed by mixture melting points, R_F values and colour reactions. A fraction of quaternary benzophenanthridines was obtained from the mother liquors in the form of non-basic pseudo-cyanides (yield of bases 10 mg or 25 mg, 0·0002 or 0·0003%, respectively), in which sanguinarine was detected using systems S_4, S_9 and S_{10} (R_F 0·80, 0·49 and 0·60, respectively) as well as chelirubine (R_F 0·90, 0·70 and 0·79, respectively, in the same solvents) in addition to trace amounts of chelerythrine (R_F 0·55, 0·14 and 0·22) and macarpine (R_F 0·65, 0·22 and 0·36). In the remaining amorphous bases of fraction AD_1 (0·08 g or 0·12 g, respectively) a base of R_F 0·15 in S_1 and 0·40 in S_2 was found in addition to protopine and allocryptopine.

From fraction AD_2 (—)-scoulerine was isolated as poorly soluble hydrochloride (yield of base 0·26 g or 0·70 g; 0·005 or 0·009% resp.). The base when crystallized from ether had m.p. 192 to 194°C (capillary), undepressed in admixture with an authentic sample, turning rapidly red in air. Mass spectrum: ion M^+ 327,1453 (theory for $C_{19}H_{21}NO_4$: 327,1470), 326 (M — 1), 178 (base peak, $C_{10}H_{12}NO_2$), 176 ($C_{10}H_{10}NO_2$), 150 ($C_9H_{10}O_2$). It was identical with the spectrum of authentic scoulerine (see[11]). The UV spectrum was also identical with the spectrum from ref.[11]. Hydrochloride (from methanol) had m.p. 232—239°C (Kofler block), undepressed with an authentic specimen; identity was confirmed by IR spectrum. Hydrobromide (from methanol) melted at 247—255°C under decomposition (Kofler block). R_F values (0·05 in S_1, 0·18 in S_2 and 0·56 in S_3) were identical with those of an authentic specimen. The bases obtained from the mother liquors after scoulerine hydrochloride crystallization (0·73 g or 0·21 g, respectively) could not be crystallized. They rapidly darkened and decomposed in air. The main components were the bases of R_F 0·08 and 0·12 in S_2 and 0·25 and 0·41 in S_3, in addition to a smaller amount of scoulerine and four other unidentified bases.

From fraction *B* after further purification yellow bases were obtained (20 mg or 12 mg; 0·0004 or 0·0002%, respectively) in which coptisine was detected as the main component (R_F 0·70 in S_5, 0·51 in S_{11} and 0·49 in S_{12}) and a small amount of corysamine (the same solvents, R_F 0·32, 0·19, 0·75) and berberine (R_F 0·53, 0·40 and 0·61 in the same solvents). Crystallization of fraction *B* (sample I) from dilute hydrochloric acid gave 7 mg of chromatographically pure coptisine chloride; it does not melt up to 270°C and decomposes under darkening (Kofler block); an authentic sample behaved in the same manner.

Fraction *E* from sample I (1·04 g) afforded 9 mg of corytuberine on crystallization from methanol (0·0002%). The amorphous residue was practically non-alkaloidal. Corytuberine hydriodide was isolated from fraction *E* of sample II (0·27 g) after separation of non-alkaloidal substances and conversion to hydriodides, (yield 30·2 mg).

Fraction *I* (6·95 g or 12·61 g, resp.) contained predominantly substances of non-alkaloidal character of which a part was separated by crystallization from chloroform (3·73 g or 1·03 g, resp.), m.p. 150—168°C (Kofler block). The remainder of fraction *I* from sample I contained traces of alkaloids only. Fraction *I* from sample II was further purified and non-alkaloidal substances were separated to afford on crystallization from methanol and methanol–ether 170 mg of corytuberine hydriodide (total yield of base in sample II is 144 mg, *i.e.* 0·002%). The corytuberine base crystallized from methanol had m.p. 238—240°C (Kofler block), unpressed with authentic preparation isolated from Corydalis cava[12]. Hydriodide (from methanol) gave leaflets melting at 210—214°C (Kofler block) or 215—217°C (capillary), undepressed in admixture with an authentic specimen (see[2]). The identity was confirmed by IR and UV spectra (see[2]), R_F values (0·71 in S_6, 0·77 in S_7, 0·40 in S_8 and 0·51 in S_{12}) and colour reactions. In the amorphous residue of fraction *I* from sample II only trace amounts of four further, probably quaternary, alkaloids of R_F

values 0·13, 0·30, 0·40 and 0·62 (in S_6) and 0·08, 0·23, 0·44 and 0·60 (in S_7) were detected in addition to residual corytuberine.

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