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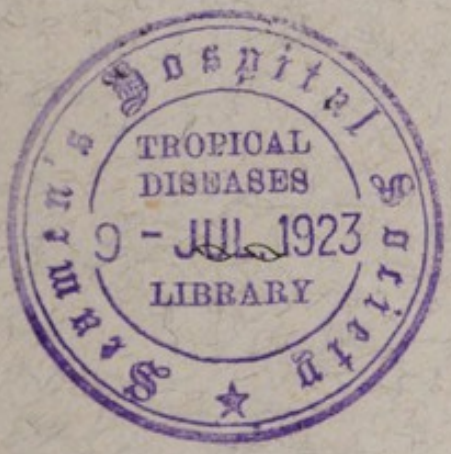

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XLII. THE CONSTITUENTS OF THE FLOWERING TOPS OF *ARTEMISIA AFRA*, JACQ.

By JOHN AUGUSTUS GOODSON.

From the Wellcome Chemical Research Laboratories.

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The genus Artemisia comprises some 350 species, of which only about 30 have been chemically examined. In most cases the investigation has been confined to the essential oil, but a few of the more important species such as wormwood, *Artemisia Absinthium* Linn., used in the preparation of absinthe, and worm-seed, *A. maritima* var. *Stechmanniana* Bess. which grows in Turkestan and is the sole source of the anthelmintic, santonin, have been more thoroughly examined. In consequence of the difficulty of obtaining santonin since 1914, other sources of this indispensable drug have been sought and in this connection attention has been given to other species of Artemisia, of which the author has examined four. *A. brevifolia* Wall. (which according to the Index Kewensis is a form of *A. maritima* Linn.) from India was found to contain santonin, as previously recorded by Greenish and Pearson [1921] and Simonsen [1921]; specimens of *A. afra* Jacq. from South Africa, *A. mexicana* Willd. from Mexico, and *A. monosperma* Delile (*A. deliliana* Bess.) from Egypt were found to contain no santonin. The closely related Egyptian plant *Santolina chamaecyparissa* was also found to be free from santonin.

Judging from these results and others previously recorded it would seem that the occurrence of santonin is restricted to species of Artemisia indigenous to East Europe and Asia, the only exception so far recorded being *A. gallica* Willd., which occurs in France, and according to Heckel and Schlagdenhauffen [1884] contains santonin. These authors, however, give no evidence for this statement and their observation has not been confirmed[1].

Of the four species examined by the author only one, *A. afra*, was available in quantity and this was fully investigated to see if it contained anything that could be regarded as a precursor or a derivative of santonin. The results given below show that this plant contains camphor, a wax-ester probably ceryl cerotate, triacontane, scopoletin and quebrachitol, none of which can be regarded as connected with santonin.

l-Camphor has been recorded in several species of Artemisia, *e.g.* in *A. Herba-alba* Ass. [Grimal, 1904], *A. cana* Pursh [Whittelsey, 1909] and *A. annua* Linn. [Yoshitomi, 1917]. In *A. afra* the camphor is dextrorotatory,

[1] Since this paper was submitted for publication a preliminary notice of a communication by Viehoever and Capen [1922] has appeared, in which it is stated that santonin has been isolated from *A. mexicana* and *A. neo-mexicana*. J. A. G.

but the rotation is much lower than that of normal *d*-camphor. Two specime were found to have $[\alpha]_D^{20} + 9{\cdot}7°$ and $[\alpha]_D^{20} + 9{\cdot}3°$ instead of $[\alpha]_D^{20} + 42{\cdot}4$ As it is usually considered that only two optically active isomerides can exi notwithstanding the fact that the camphor molecule contains two asym metric carbon atoms, and as camphor is not easily racemised, it would appe that both *d*- and *l*-camphor are present in *A. afra*. It may be noted tha inactive camphor has been found in *Chrysanthemum sinense* var. *japonicu* [Keimatsu, 1909].

Scopoletin and quebrachitol have not been recorded previously in th genus Artemisia or even in the natural order Compositae. The former ha been found in *Atropa Belladonna* Linn. [Kunz, 1885], *Fabiana imbricata* Rui et Pav. [Kunz-Krause, 1899] and *Scopolia japonica* Maxim. [Eykman, 1884 of the natural order Solanaceae; *Ipomoea purga* Hayne (Convolvulaceae [Power and Rogerson, 1910]; *Gelsemium sempervirens* Ait. (Loganiaceae [Moore, 1910] and *Prunus serotina* Ehrh. (Rosaceae) [Power and Moore, 1909 Quebrachitol has only been found in four other plants, viz. *Aspidosperm quebracho* Schlect (Apocyanaceae) [Tanret, 1889]; *Grevillea robusta* A. Cun (Proteaceae) [Bourquelot and Fichtenholz, 1912]; *Heterodendrum oleaefolium* Desf. (Sapindaceae) [Petrie, 1918] and *Hevea brasiliensis* Muell. (Euphorbia ceae) [Pickles and Whitfield, 1911], all of which belong to different natura orders. The other components ceryl cerotate and triacontane are fairly widely distributed in plants.

Experimental.

For the material used in this investigation the author is indebted to Mr I. B. Pole Evans, Chief of the Division of Botany, Union of South Africa It consisted of the flowering tops of the plant including stems, leaves and florets.

When extracted with Prollius's fluid it yielded a mere trace of alkaloid and furnished the following percentages of extract on exhaustion in a Soxhlet apparatus with solvents in the order named: petroleum (b.p. 35–60°), 7·0; ether, 9·5; chloroform, 2·1; ethyl acetate, 3·4; alcohol, 15·5. Special search was made for santonin with negative results. For the purpose of a more complete examination a quantity (11·1 kilograms) was extracted in succession with hot solvents, petroleum (b.p. 35–60°), ether and alcohol. The alcoholic extract was further fractionated by drying on a quantity of the flowering tops previously exhausted with petroleum and ether and re-extracting hot with chloroform, ethyl acetate and alcohol in succession. The petroleum extract on distillation in steam and extraction of the distillate with ether yielded 55·2 g. of essential oil; a further 28·6 g. was subsequently obtained from the ether extract, equivalent in all to 0·75 % by weight of the flowering tops.

The material left behind in the distillation flask on boiling with petroleum (b.p. 35 to 60°), deposited on cooling about 81 g. of crude wax-ester melting at 74–76°. The residue left on removal of the petroleum was boiled with ether

and this solution on cooling gave 17 g. of crude hydrocarbon, melting at 62 to 66°. The ethereal solution was then extracted with dilute hydrochloric acid, but yielded no alkaloid; it still contained some free and combined fatty acids, which were not investigated, and some unsaponifiable matter, which appeared to contain a sterol giving a red coloration with acetic anhydride and sulphuric acid.

Examination of the Essential Oil. The oil possessed the odour of camphor, had a specific gravity 0·9453 at 15°/15° and specific rotation $[\alpha]_D^{15} + 5{\cdot}8°$. On washing with solutions of sodium carbonate, sodium hydroxide and sodium bisulphite (saturated), it lost to each quantities of material too small to be investigated in detail. The acids extracted by sodium carbonate were fractionally precipitated as silver salts, the fractions containing 24·7, 34·9, 38·6, 39·9 and 41·3 % of silver respectively. Silver pelargonate, $C_8H_{17}COOAg$ requires Ag = 40·4. The saponification value of the oil before acetylation was 33·9 and after acetylation 73·9.

On distillation the following fractions per cent were obtained (1) below 180°/760 mm., 31·8; (2) below 100°/25 mm., 27·5; (3) at 100–120°/25 mm., 12·1; (4) at 120–140°/25 mm., 12·3; (5) at 140–180°/25 mm., 8·0; (6) and above 180°/25 mm., 7·7.

Isolation of Camphor. Fractions (2) and (3) on standing deposited camphor, a further quantity of which separated on redistilling the fractions and freezing the distillates with solid carbon dioxide, the total quantity obtained amounting to 13·5 % of the crude oil, but this does not represent the total amount of camphor in the oil as much still remained in the various fractions. The crude camphor was recrystallised from dilute alcohol until its melting point was constant at 178° (corr.) and showed no depression of melting point on admixture with natural *d*-camphor melting at 180° (corr.). The specific rotation was low, being only $[\alpha]_D^{20} + 9{\cdot}7°$ in 95 % alcohol ($\alpha_D^{20} = + 0{\cdot}98°$, $l = 1$ dcm. C = 10·148), that of natural *d*-camphor used for comparison being $[\alpha]_D^{20} + 42{\cdot}4°$ ($\alpha_D^{20} = + 4{\cdot}35°$, $l = 1$ dcm., C = 10·261). Found C = 78·9; H = 10·5. Calculated for camphor, $C_{10}H_{16}O$, C = 78·9; H = 10·6.

The oxime was prepared and after recrystallisation melted at 118–119° (corr.), the melting point remaining unchanged on admixture with camphor-oxime prepared from natural *d*-camphor. It was laevo-rotatory $[\alpha]_D - 3{\cdot}4°$ ($\alpha_D = - 0{\cdot}16°$, $l = 0{\cdot}5$ dcm., C = 9·296). The semicarbazone after recrystallisation from alcohol melted with decomposition at 241° (246° corr.) and when mixed with camphor-semicarbazone prepared from natural *d*-camphor, m.p. 246° (corr.) with decomposition, it melted at 242° (247° corr.). The melting point of the semicarbazone of *d*-camphor is usually given in the literature as 236–238°, but this is undoubtedly too low. (Found C = 63·4; H = 9·4. Calculated for camphor-semicarbazone, $C_{11}H_{19}N_3O$, C = 63·1; H = 9·2.)

Examination of wax-ester. The wax-ester was recrystallised many times from ethyl acetate or petroleum and then melted constantly at 79°, although

it appeared still to contain a small quantity of hydrocarbon. From the analyses of the ester and its hydrolytic products, it would appear to be ceryl cerotate or a closely related ester. (Found C = 82·5, 82·5; H = 13·5, 13·7. Calculated for ceryl cerotate, $C_{26}H_{53}COOC_{25}H_{51}$, C = 82·0; H = 13·8.)

The alcohol obtained on hydrolysis melted at 74°, and gave an acetyl derivative melting at 64–66°. Ceryl alcohol melts at 81°, and ceryl acetate at 64·5°. (Found C = 81·6, 81·5; H = 14·2, 13·9. Calculated for ceryl alcohol, $C_{26}H_{54}O$, C = 81·6; H = 14·2.)

(Found C = 79·0; H = 13·3. Calculated for ceryl acetate, $CH_3COOC_{26}H_{53}$, C = 79·2; H = 13·3.)

The fatty acid produced on hydrolysis melted at 76°. (Found C = 78·7, 78·8; H = 13·3, 13·5. Calculated for cerotic acid, $C_{26}H_{52}O_2$, C = 78·7; H = 13·2; m.p. 82°.)

Isolation of Triacontane. The crude hydrocarbon was distilled under reduced pressure and recrystallised several times from ethyl acetate and petroleum until it melted constantly at 66°. (Found C = 84·9; H = 14·9. Calculated for triacontane, $C_{30}H_{62}$, C = 85·2; H = 14·8; m.p. 65·5°.)

After removal of the essential oil, wax-ester and hydrocarbon from the ether extract, the latter was extracted with dilute hydrochloric acid, which removed no alkaloid or other basic material and then with sodium carbonate solution, followed by potassium hydroxide solution.

Isolation of Scopoletin. The sodium carbonate extract was acidified with hydrochloric acid, and extracted with ether. The ethereal solution on concentration deposited a crystalline substance, a further quantity of which was obtained by extracting the dilute hydrochloric acid extract of the original ether extract with ether. The substance was purified by recrystallisation from ethyl acetate, yielding 2 g. of pure material, which formed pale yellow needles and dissolved in sodium carbonate solution giving a solution possessing a striking blue fluorescence. It melted at 203° (208° corr.) the melting point being uninfluenced on admixture with scopoletin. (Found C = 62·4, 62·4; H = 4·2, 4·5. Calculated for scopoletin (4-hydroxy-5-methoxycoumarin), $C_{10}H_8O_4$, C = 62·5, H = 4·2.)

The chloroform extract yielded no crystalline substance and dilute hydrochloric acid removed from it only a trace of material giving alkaloid reactions.

Isolation of Quebrachitol (Methyl l-inositol). The residues of the ethyl acetate, and alcoholic extracts, after concentration, deposited a mixture of resinous matter and crystals, which was extracted with water, the solution was boiled with animal charcoal, filtered, and concentrated and finally alcohol was added when a quantity of crude methyl-*l*-inositol crystallised out corresponding to 0·43 % of the flowering tops used. After several recrystallisations it melted constantly at 194° (corr.), and had a specific rotation $[\alpha]_D$ − 81·6° (α_D = − 8·16°, l = 1 dcm., C = 10·0). Found C = 43·2, 43·4; H = 7·0, 7·3. Calculated for quebrachitol, $CH_3OC_6H_6(OH)_5$, C = 43·3; H = 7·3.

The acetyl derivative, prepared by the action of acetic anhydride in presence of pyridine, was recrystallised from ethyl acetate and obtained in rosettes of needles, melting at 94–95°. (Found C = 50·8; H = 6·1. Calculated for penta-acetylmethylinositol, $CH_3OC_6H_6(OOC.CH_3)_5$, C = 50·5; H = 5·9.)

There is no published record of previous chemical work on *Artemisia afra* but the author desires to state that Messrs H. W. B. Clewer, and R. R. Baxter have made preliminary examinations of the plant in these laboratories, and their records, which include the isolation of camphor and of the crystalline substance now shown to be quebrachitol, have been available to him.

In conclusion, the author desires to express his warmest thanks to Dr T. A. Henry for his advice and criticism throughout the course of the work.

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