

high boiling liquid, representing 33.76 per cent of the oil, constituted mainly bornyl acetate and the sesquiterpene, lævo-cadinene.

Acetic acid was the principal combined acid with isovaleric acid possibly present in small quantities.

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THE PIGMENTS CONTAINED IN THE BARK OF THE ROOT OF CELASTRUS SCANDENS.*

BY O. GISVOLD.¹

1. CELASTROL.

At one time some investigators thought that the chief pigment found in the outer bark of the root of *Celastrus scandens* was β -carotene. β -Carotene is of great importance because of its use as a standard for vitamin A, and therefore confirmation of its existence in a plant from which it might be easily isolated and purified was deemed advisable.

EXPERIMENTAL.

The material investigated was collected near Savage, Minn. The outer bark of the freshly collected roots of *Celastrus scandens* was readily removed with a vegetable grater. The bark thus obtained was ground and extracted with Skelly-solve B. The principal pigment contained in the bark was more soluble than other pigments present in lesser quantities, and therefore could be separated from them by fractional extraction. The first Skelly-solve B. extract contained so much pigment that it separated during the process of extraction. Upon prolonged extraction with fresh solvent, other pigments also separated. These varied in color from orange to yellow and some were even brown.

Celastrol.—Approximately 40 Gm. of the chief pigment were obtained as ruby-red cubes. They were recrystallized from a mixture of isopropyl ether and Skelly-solve B. The crystals melted apparently at 205° C. although there was evidence of decomposition. Additional recrystallizations failed to raise the observed melting point. Further investigations have shown that this compound contains hydroxyl groups and therefore the name celastrol is proposed. Celastrol is soluble in the fat solvents and in ethyl and methyl alcohols. It can be shaken from an ether solution with aqueous sodium hydroxide or sodium carbonate. The sodium salt forms a very dark red solution. The pigment cannot be shaken from ether by means of aqueous sodium bicarbonate. It forms a barium salt which is insoluble in methyl alcohol. Celastrol can be extracted from petroleum ether with 60 per cent or stronger aqueous methyl alcohol. The specific rotation of celastrol was very difficult to obtain because of the exceedingly dark-colored solutions.

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The original pigment as well as the derivatives made from it were dried at 100° C. over phosphorus pentoxide in a vacuum. The results of some of the analyses indicate that not all of the solvent was removed by this treatment.

Analysis— $[\alpha]_D^{25} = 0$ (in CHCl_3)

$\text{C}_{23}\text{H}_{36}\text{O}_3$	Calculated	C 76.69	H 10.00
	Found	C 76.66, 76.59	H 9.08, 8.65

Celastrol Acetate.—The acetate was prepared by heating celastrol with acetic anhydride and pyridine for one hour on a steam-bath. The acetate was yellow and melted approximately at 241° C.

Analysis— $[\alpha]_D^{25} = -54.2$ (in CHCl_3)

$\text{C}_{26}\text{H}_{34}\text{O}_5$	Calculated	C 73.00	H 8.00
	Found	C 73.27, 73.31	H 7.95, 8.30

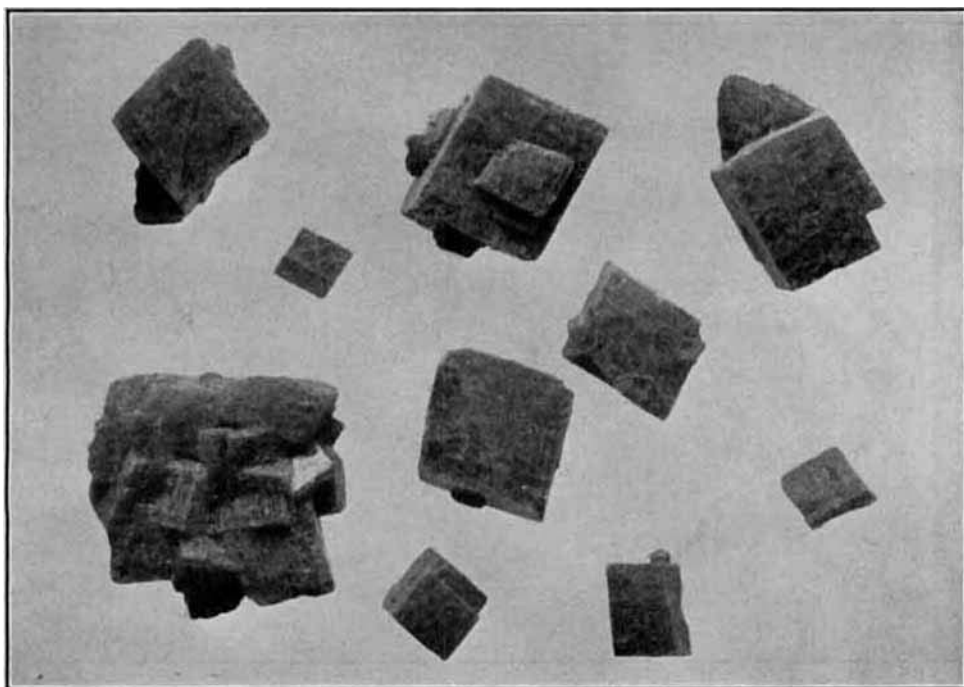


Fig. 1.—Celastrol.

Methyl Celastrol.—The methylated derivative was prepared by dissolving celastrol in dry ether and treating it with an excess of diazomethane. Methylation took place very rapidly. The derivative crystallized as orange needles from a mixture of ether and petroleum ether. M. p. 217.5–218° C.

Analysis— OCH_3

$\text{C}_{23}\text{H}_{37}\text{O}_3$	Calculated	8.71
	Found	9.19, 8.83; av. 9.01
	Molecular weight, rast	347

Methyl Acetyl Celastrol.—The yellow acetate was methylated by means of diazomethane in dry ether. The yellow derivative was not obtained in crystalline form from a mixture of ether and Skelly-solve B. M. p. 132–133° C. After the compound was dried in a vacuum over phos-

phorus pentoxide, it gave the following methoxyl content, 8.99 and 9.27 per cent, respectively. These values appear to be higher than the theoretical. This may be due to traces of ether which could not be removed under the conditions of the experiment. However, the methoxyl content indicates that one methyl group was introduced into acetyl celastrol.

Acetyl Methyl Celastrol.—Methyl celastrol was acetylated with a mixture of acetic anhydride and pyridine. A yellow amorphous compound was obtained from a mixture of ether and Skelly-solve B. M. p. 132° C. The methoxyl content was 9.18 and 9.15 per cent, respectively.

Oxidation with Potassium Permanganate.—Five grams of celastrol were oxidized with cold aqueous alkaline permanganate according to the technique of Kuhn and Deutsch (1). Difficulty was encountered in attempting to obtain a crystalline oxidation fragment. The following technique overcame this difficulty. Purified sand was impregnated with the crude oxidation mixture and then extracted with Skelly-solve B. The Skelly-solve B. soluble fraction was crystallized only from dry ether. M. p. 252° C.

Reduction of Celastrol.—Celastrol was reduced in alcohol at 190° C. with Raney nickel as a catalyst.¹ One mole of hydrogen was absorbed by one mole of celastrol. A colorless solution

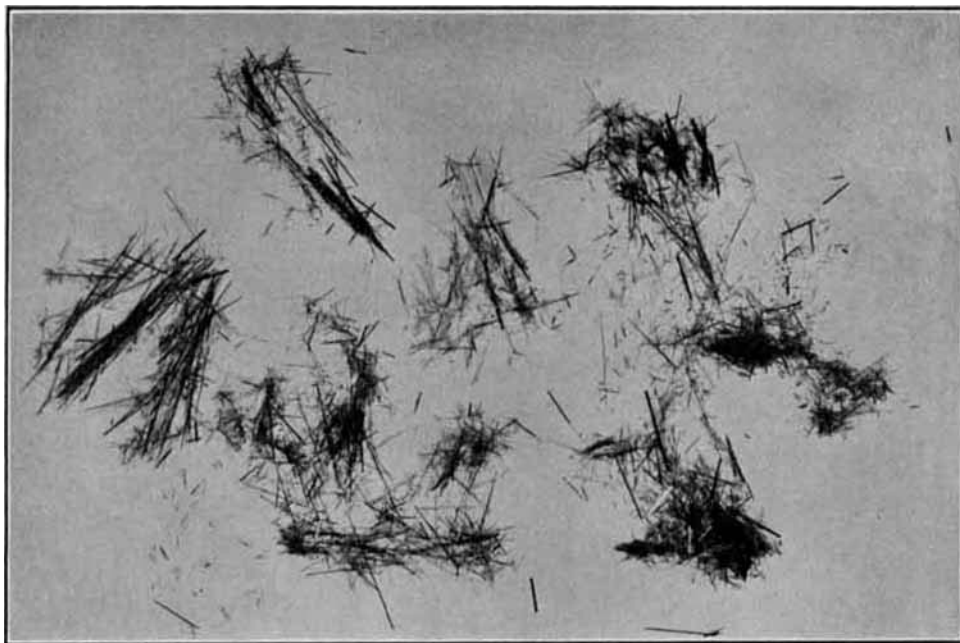


Fig. 2 —Methyl Celastrol.

was obtained which soon became red upon standing in a beaker in the presence of the catalyst. An attempt to obtain a crystalline reduction product resulted in the recovery of ruby-red cubes. M. p. 203° C. When mixed with celastrol, no change in melting point was observed. The mother liquors yielded a very small amount of colorless needles (microscopic). These were not separated from the ruby-red cubes.

Iodine Number.—Wijs reagent (iodine and chlorine in glacial acetic acid) was used for the determination of the iodine number. The reagent was allowed to remain in contact with celastrol for twenty-four hours.

Analysis— $C_{20}H_{32}O_3$ with three double bonds.

Calculated	236
Found	233, 231, 230

¹ By Homer Adkins, University of Wisconsin.

Oxime.—An attempt to prepare an oxime according to the technique of Vavon and Anziani (2) failed.

Color Reactions.—Celastrol and methyl celastrol gave a green color with ferric chloride. Acetyl celastrol, acetyl methyl and methyl acetyl celastrols gave no color with ferric chloride.

SUMMARY.

The bark of the root of *Celastrus scandens* contains no β -carotene. A red pigment has been isolated and named celastrol. Some of its physical properties and also those of some of its derivatives have been reported.

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NATURAL AND ARTIFICIAL CALAMINES FROM THE PHARMACEUTICAL, CHEMICAL AND PHARMACOLOGICAL STANDPOINTS.*¹

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INTRODUCTION.

The investigation of calamines began in 1803 when James Smithson (1) first distinguished chemically the differences between the silicate and the carbonate of zinc. Since then calamines have presented a challenging problem to pharmacists.

Prepared calamine N. F. VI is 98 per cent zinc oxide colored pink by the addition of a small amount of ferric oxide. It is extensively used for skin affections in the form of lotions and ointments. The question has been raised as to its merits over those of zinc oxide, and also whether the native calamine, generally described as impure zinc carbonate, and also precipitated zinc carbonate might not be better than the oxides.

This study was begun with the view of settling some of these questions.

HISTORY AND NOMENCLATURE.

There has been considerable confusion in the names applied to calamine. In the early history the oxide, carbonate and silicate of zinc were all known by the term cadmia or cadmea (4). At the present time, a native carbonate of zinc is called calamine by British mineralogists and smithsonite by Americans. The silicate of zinc is termed hemimorphite or electric calamine by the British, and calamine by the American mineralogists. In pharmacy, however, only the zinc carbonate has ever been recognized as calamine in both America and England.

The distinction between the silicate and carbonate of zinc by Smithson (1) in 1803 and the later work of Beudant (3) stimulated much interest in the commercial calamines. Following the work of Brett in 1837 many British and American workers turned to the analysis of them (6). The results in most cases showed that what appeared on the market as native zinc carbonate was barium sulfate colored with iron oxide. This situation was true in the British Isles, on the Con-

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