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HYDROLYSABLE TANNINS HAVING ENANTIOMERIC DEHYDROHEXAHYDROXYDIPHENOYL GROUP: REVISED STRUCTURE OF TERCHEBIN AND STRUCTURE OF GRANATIN B

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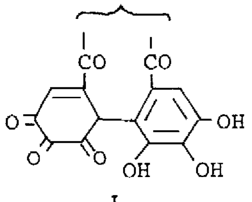
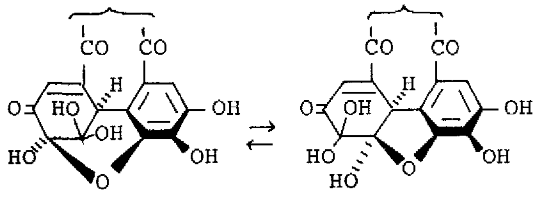
Summary: Revised structure of terchebin is shown by II-B. Granatin B, a new ellagitannin, has structure V in which partial structure Ic⇄Id is enantiomeric to Ia⇄Ib in II-B and geraniin.

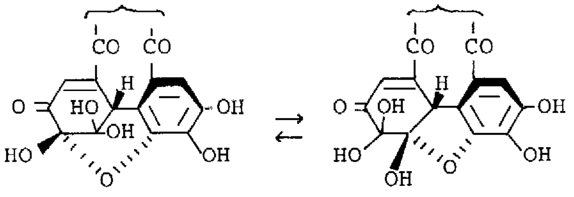
Although vegetable tannins are generally polyphenols, there was a view that quinoids are intermediates in the tanning process[1]. Dehydrohexahydroxydiphenoyl (DHHDP) group (I) which is present as an equilibrium mixture Ia⇄Ib in some ellagitannins[2], should be participating in the activities of these tannins. Biogenetically I may be one of the products of oxidation of polyhydroxydiphenoyl group which is formed by oxidative coupling of galloyl group[3], or conversely an intermediate product between the biphenyl group and its precursor produced by carbohydrate-type *condensation*[4].



I



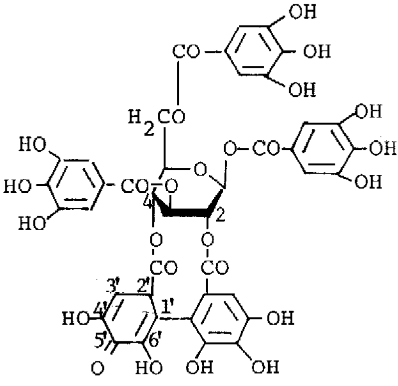
Ia Ib



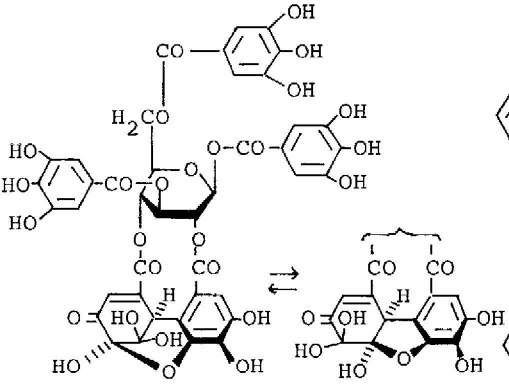
Ic Id

Structure of terchebin isolated from myrobalans (fruit of <u>Terminalia chebula</u>) had been reported to be II-A[5]. However, a further evidence should be required for the cyclohexadienone moiety in II-A which exists without tautomerising to trihydroxyphenyl group. The location of this group at O-4 of glucose, not at O-2, also lacks proof.

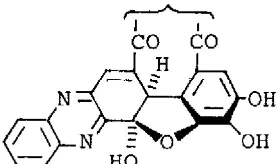
We have now found that structure of terchebin is shown by II-B which has Ia⇄Ib as a partial structure. We have also found that an enantiomeric partial structure Ic⇄Id is present in a new ellagitannin named granatin B (V).



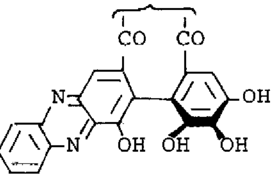
II-A



II-B



III



IV

Terchebin in the present investigation was isolated practically in the same way as reported previously[6], with partial improvement at the final stage by application of droplet countercurrent chromatography, and identified by ^{1}H-NMR spectra, optical rotations, paper chromatography, and colour reactions.

One of the bases of presuming dihydroxycyclohexadienone instead of cyclohexenetrione in II-A was that chloroellagic acid was not isolated upon hydrolysis of terchebin in concentrated hydrochloric acid[6]. However, we have found that terchebin, as well as geraniin which has partial structure Ia$\rightleftarrows$Ib[2], show in the mass spectrum measured after methylation of the precipitate occurred upon the hydrolysis, the ion peaks of tetra-O-methylchloroellagic acid (M$^+$, m/e 392; M$^+$+2, m/e 394) along with the peaks due to tetra-O-methylellagic acid (M$^+$, m/e 358). Another basis in support of structure II-A was that hydrogenized terchebin decolourized Tillmans' reagent[7]. However, we have found that hydrogenized geraniin also decolourizes Tillmans' reagent.

The ^{1}H-NMR spectrum of terchebin shows protons at δ4.66 (1/2H, d, J=1.3 Hz), 4.96 (1/2H, s), 6.24 (1/2H, d, J=1.3 Hz) and 6.48 (1/2H, s), which were formerly regarded as due to H-2' and H-3' in the epimers concerning C-2' in structure II-A[5]. However, now these protons are assignable to H-1' and H-3' in structure II-B based on analogy of the peak patterns to those of geraniin.

The carbon peaks in the ^{13}C-NMR spectrum assignable to hydrated cyclohexenetrione moiety in the partial structure Ia$\rightleftarrows$Ib are as follows (acetone-d_6, δ): C-1' (46.5$\rightleftarrows$52.4), C-2' (155.2$\rightleftarrows$150.0), C-3' (130.0$\rightleftarrows$126.5), C-4' (193.0$\rightleftarrows$195.6), C-5' (96.8$\rightleftarrows$93.1) and C-6' (93.1$\rightleftarrows$109.7). These paeks which are analogous to those of geraniin and mallotusinic acid[2], exclude structure II-A.

Upon condensation with o-phenylenediamine, terchebin yielded a product III, which was converted to another product IV in an acidic solution. These products are analogues of "phenazine A" and "phenazine B" derived from geraniin, as shown by the ^{1}H-NMR and ^{13}C-NMR spectra. Hydrolysis of these products yielded a precipitate which was found to be identical as "phenazine C" obtained from geraniin[8]. The supernatant liquor gave an amorphous powder which was identified as 1,3,6-trigalloyl-β-D-glucopyranose.

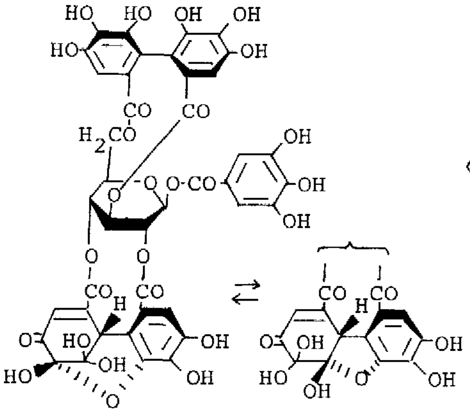
These results indicate revised structure II-B for terchebin. The orientation of DHHDP and the configuration at C-1' in this structure are based on the upfield shift of H-1 (δ6.65→6.26) upon the aromatization in the phenazine derivative, as this shift shows analogy of the relative spatial locations of H-1 of glucopyranose and cyclohexenetrione in terchebin to those in geraniin[2,9].

The fruit rind of pomegranate (Punica granatum) has been used as an astringent drug in China. In addition to punicalagin and punicalin[10], we have isolated a new ellagitannin named granatin B (V) by droplet countercurrent chromatography of ethyl acetate soluble fraction.

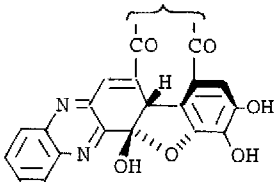
Granatin B (V) formed yellow crystals, $C_{41}H_{28}O_{27}\cdot 8H_{2}O$, from water, which show mutarotation of reversed direction of that of geraniin, ($[\alpha]_{D}^{28}$ $-109° \rightarrow -123°$, 4 hr, acetone-water, 9:1). The ^{1}H-NMR and ^{13}C-NMR spectra of V before and after the equilibration showed practically all of the peaks corresponding to those of geraniin, with small difference of the chemical shifts.

Condensation of V with o-phenylenediamine gave products, VI and VII, which were shown by the ^{1}H-NMR and ^{13}C-NMR spectra to be isomeric to "phenazine A" and "phenazine B". The upfield shift of H-1 of glucose in the ^{1}H-NMR spectrum was not observed in VII. Upon hydrolysis, these derivatives gave "phenazine C" and corilagin in analogous way as "phenazine A" and "phenazine B"[8].

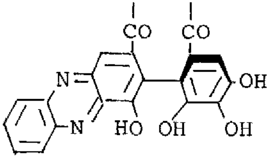
Methylation of VII overnight with diazomethane in a mixture of moist ether and methanol gave a tetradeca-O-methyl derivative VIII, which gave monoacetate IX. The H-4 peak of the glucose moiety, which was hidden by other protons in VIII, showed downfield shift to δ5.64 in IX, while the difference of the chemical shift of H-2 in VIII and IX was only 0.02 ppm. These data indicate that the ester linkage on O-4 of the glucose moiety was methanolysed upon the methylation of VII. Hydrolysis of IX in 10% hydrochloric acid, followed by extraction with chloroform, and fractionation by preparative TLC, gave an acid X. The location of free carboxyl group in X is regarded as at C-2'', based on the comparison of the downfield shift of H-3''(δ7.36→7.44) in the ^{1}H-NMR spectrum, induced on addition of pyridine-d_{5} (5%) into the deuteriochloroform solution, with the shifts in the analogues[9]. These data indicate structure VIII for the



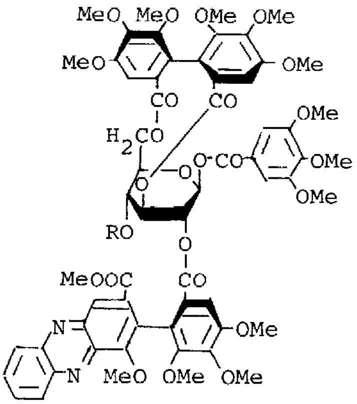
V



VI

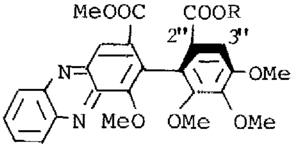


VII

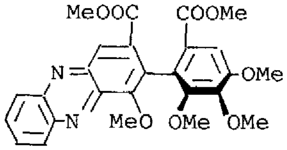


VIII: R=H

IX: R=Ac



X: R=H, XI: R=Me



XII

product of methylation of VII, and show that cyclohexenetrione moiety in DHHDP in granatin B links to O-4 of the glucose moiety in analogous way as in geraniin.

The hydrolysis product X gave dimethyl ester XI ($[\alpha]_D^{23}$ -39°, ethanol, c=1.0), which is the atropisomer of XII ($[\alpha]_D^{23}$ +37°, ethanol, c=1.2) derived from geraniin. The stereostructure and the absolute configurations of granatin B are therefore represented by V.

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