Absolute Configuration of *epi*-Rhododendrin and (−)-Rhododendrol [= (−)-Betuligenol] and X-Ray Crystal and Molecular Structure of Rhododendrin [= Betuloside], a Hepatoprotective Constituent of *Taxus baccata*[1]

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Rhododendrin (= betuloside) has been isolated from the leaves of *Taxus baccata* L. From its X-ray diffraction studies, the absolute configuration at the chiral centre in the aglucone portion has been found to be *R*. These results establish the stereochemical assignments to different samples of this glucoside isolated from different plants. Our sample of rhododendrin exhibited hepatoprotective activity against two hepatotoxins in rats.

Different *Taxus* species have evoked a good deal of interest among phytochemists in recent years because they have been found to possess a range of biological activities, *i.e.* cytotoxic and antileukaemic;[2] sedative and antiseptic;[3] tranquilising,[4] and antimitotic.[5] Khan *et al.*[6] have isolated betuloside as the major component of the aqueous extract of the leaves of *Taxus baccata*; in view of the fact that the aqueous extract possesses good tranquilising activity,[4] we planned to carry out a detailed study on the structure and biological activities of betuloside. On close scrutiny of the literature, we found an interesting series of papers relating to the occurrence and structure of this compound. This glycoside, with the name rhododendrin, along with its aglucone rhododendrol, was isolated for the first time from the leaves of *Rhododendron chrysanthum* Linn. in 1901.[7] Later, a similar glucoside, named betuloside, was isolated from the bark of the white birch, *Betula alba* L.[8,9] Rhododendrin isolated from *Rhododendron fauriae* var. *rufescens*,[10] and its aglucone rhododendrol, were subsequently shown to be identical with betuloside and betuligenol, respectively.[11] More recently the distribution of rhododendrin in the genera *Rhododendron*[12–14] and *Betula*[15] has been surveyed and it has also been found in *Bergenia* species,[12] *Abies webbiana* Lindl.,[16] *Rhodiola* species,[17] *Alnus glutinosa* Gaertn.,[18] *Taxus baccata* L.[6] and *Cotyledon wallichii*.[19]

The biosynthesis of rhododendrin has been studied[18] and it was established that it is formed through the phenylpropane pathway *via* *p*-coumaryl alcohol, dihydro-*p*-coumaryl alcohol, and *C*-methylation of the γ-C-atom of the C_6–C_3 unit with methionine supplying the methyl group. It was demonstrated that the *pro*-(*S*) hydrogen atom of dihydro-*p*-coumaryl alcohol is replaced stereospecifically by the methyl group. There is ambiguity about the configuration at C-2; however, in the previously reported structural formula of rhododendrin the configuration at this chiral centre was depicted as *S*.[18]

The aglucone, (−)-rhododendrol, is found to co-occur in many species, but it is interesting that (+)-rhododendrol has been isolated from *Rhododendron maximum*.[20] Furthermore (+)-rhododendrol and its glucoside *epi*-rhododendrin were isolated in 1978 from *Acer nikoense* MAXIM. and were proposed to have the (2*S*)-configuration from both the empirical rule on optical rotation–chirality relations[21] and ^{13}C NMR studies.[22]

In the light of these different findings concerning configuration, it was of interest to carry out an X-ray study of rhododendrin (betuloside) isolated by us from *Taxus baccata* L. This work, and the conclusions concerning the configuration, are reported in the present paper.

Table 1 Bond angles (°) for rhododendrin

Atom 1, 2 and 3	Angle	Atom 1, 2 and 3	Angle
C(1)–O(1)–C(5)	111.0(1)	C(1)–O(6)–C(7)	112.3(1)
O(1)–C(1)–C(2)	109.7(1)	O(6)–C(7)–C(8)	109.0(2)
O(1)–C(1)–O(6)	108.6(1)	O(6)–C(7)–C(16)	109.3(1)
C(2)–C(1)–O(6)	108.8(1)	C(8)–C(7)–C(16)	112.2(2)
C(1)–C(2)–C(3)	108.7(1)	C(7)–C(8)–C(9)	113.4(2)
C(1)–C(2)–O(2)	111.1(1)	C(8)–C(9)–C(10)	114.4(2)
C(3)–C(2)–O(2)	108.8(1)	C(9)–C(10)–C(11)	120.1(2)
C(2)–C(3)–C(4)	110.5(1)	C(9)–C(10)–C(15)	122.3(2)
C(2)–C(3)–O(3)	111.4(1)	C(11)–C(10)–C(15)	117.6(2)
C(4)–C(3)–O(3)	112.2(1)	C(10)–C(11)–C(12)	122.1(2)
C(3)–C(4)–C(5)	110.3(1)	C(11)–C(12)–C(13)	119.8(2)
C(3)–C(4)–O(4)	112.1(1)	C(12)–C(13)–C(14)	119.6(2)
C(5)–C(4)–O(4)	111.4(1)	C(12)–C(13)–O(7)	118.8(2)
O(1)–C(5)–C(4)	108.2(1)	C(14)–C(13)–O(7)	121.7(2)
O(1)–C(5)–C(6)	108.0(1)	C(13)–C(14)–C(15)	120.2(2)
C(4)–C(5)–C(6)	113.5(1)	C(10)–C(15)–C(14)	120.8(2)
C(5)–C(6)–O(5)	112.4(1)		

Numbers in parentheses are estimated standard deviations in the least significant digits.

Table 2 Bond distances (Å) in rhododendrin

Atom 1 and 2	Distance	Atom 1 and 2	Distance
O(1)–C(1)	1.421(2)	O(6)–C(7)	1.455(2)
O(1)–C(5)	1.435(2)	C(7)–C(8)	1.519(2)
C(1)–C(2)	1.523(2)	C(7)–C(16)	1.517(3)
C(1)–O(6)	1.384(2)	C(8)–C(9)	1.528(3)
C(2)–C(3)	1.533(2)	C(9)–C(10)	1.520(2)
C(2)–O(2)	1.411(2)	C(10)–C(11)	1.388(3)
C(3)–C(4)	1.522(2)	C(10)–C(15)	1.403(3)
C(3)–O(3)	1.423(2)	C(11)–C(12)	1.388(3)
C(4)–C(5)	1.544(2)	C(12)–C(13)	1.379(3)
C(4)–O(4)	1.422(2)	C(13)–C(14)	1.397(3)
C(5)–C(6)	1.522(2)	C(13)–O(7)	1.379(2)
C(6)–O(5)	1.439(2)	C(14)–C(15)	1.391(2)

Numbers in parentheses are estimated standard deviations in the least significant digits.

Table 3 Atomic co-ordinates and their estimated standard deviations in rhododendrin

Atom	*x*	*y*	*z*
O(1)	0.671 9(3)	0.592 9(2)	0.653 84(5)
C(1)	0.521 9(4)	0.454 9(3)	0.657 16(7)
C(2)	0.611 9(4)	0.306 9(3)	0.682 92(7)
C(3)	0.665 6(4)	0.380 1(3)	0.724 85(7)
C(4)	0.805 6(4)	0.541 8(3)	0.721 11(6)
C(5)	0.705 0(4)	0.677 0(3)	0.692 15(6)
C(6)	0.841 1(4)	0.838 9(3)	0.685 11(7)
O(2)	0.465 1(3)	0.169 0(2)	0.687 43(5)
O(3)	0.756 3(3)	0.248 6(2)	0.750 02(5)
O(4)	0.851 5(3)	0.618 1(3)	0.759 38(5)
O(5)	1.055 7(3)	0.794 3(2)	0.675 55(5)
O(6)	0.480 2(3)	0.390 5(2)	0.618 85(4)
C(7)	0.327 8(4)	0.497 9(3)	0.597 22(7)
C(8)	0.375 3(4)	0.489 6(4)	0.552 26(7)
C(9)	0.602 5(5)	0.537 7(4)	0.541 89(7)
C(10)	0.652 0(5)	0.536 0(4)	0.496 93(7)
C(11)	0.850 7(5)	0.486 7(4)	0.483 55(8)
C(12)	0.903 5(5)	0.485 9(4)	0.442 87(7)
C(13)	0.756 5(5)	0.535 1(3)	0.414 38(7)
C(14)	0.555 7(5)	0.587 1(4)	0.426 82(7)
C(15)	0.504 6(5)	0.588 6(4)	0.467 73(7)
C(16)	0.107 2(4)	0.434 0(4)	0.606 89(7)
O(7)	0.812 8(3)	0.532 7(3)	0.374 10(5)

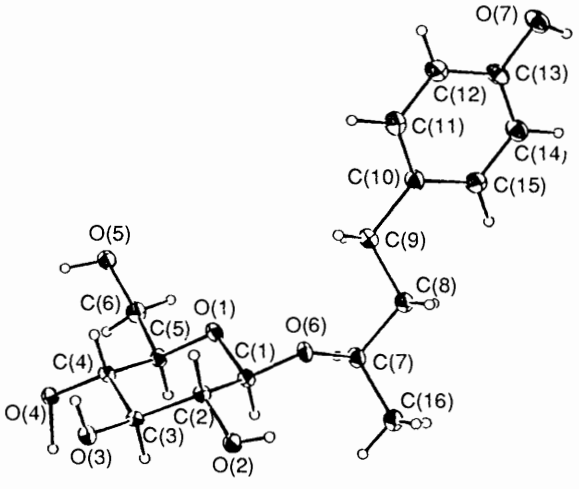


Fig. 1 Computer-generated perspective drawing of the X-ray molecular structure of rhododendrin

Results and Discussion

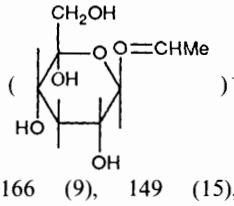
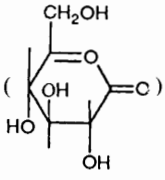
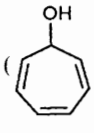
From the work of Sosa,[9] it is known that rhododendrin can be hydrolysed by hydrochloric acid and by the β-D-glucosidase emulsin to give D-glucose. With this knowledge it should be possible to determine the absolute configuration of the chiral aliphatic centre C-2 by a single-crystal X-ray analysis of rhododendrin. The rhododendrin used was isolated from *Taxus baccata* and its ^{13}C NMR spectrum established that the carbohydrate moiety is glucopyranose and confirmed that the glucosidic linkage is β. The bond distances and the bond angles (Tables 1–3) determined by X-ray diffraction confirmed that rhododendrin is a β-glucopyranoside and the molecular geometry of the glucose moiety agrees well with the results obtained from crystal-structure determinations of D-glucose.[23,24] From the chemical work previously carried out we know that the glucosyl moiety has the D-configuration. With this firmly established, the X-ray molecular structure (Fig. 1) reveals that the chiral aliphatic atom C-2, to which the β-D-glucopyranosyl moiety is attached, has the (2*R*)-configuration. The crystal structure is stabilised through an extensive hydrogen-bond system. A stereo-pair showing the crystal packing is shown in Fig. 2. Every rhododendrin molecule is interacting with five other molecules as shown in the drawing. It is likely that the conformation of rhododendrin in the crystal is determined by these interactions.

In conclusion, Scheme 1 exhibits the absolute configuration for rhododendrin, *epi*-rhododendrin, (+)- and (−)-rhododendrol.

Our sample of betuloside exhibited good hepatobiliary effect against two hepatotoxins in rats. At a dose of 10 mg kg^{-1} it reversed the enhanced galactosamine-induced alkaline phosphatase (ALP) level by 40%, whereas at a dose of 25 mg kg^{-1} it was 100% effective in normalising the thioacetamide-induced glutamate dehydrogenase (GDH)-enhanced level (Table 4). It is well known that the biological activities of chiral compounds depend on their configuration, and so we feel that this work should be of interest as it deals with the determination of configuration of a biologically active natural product.

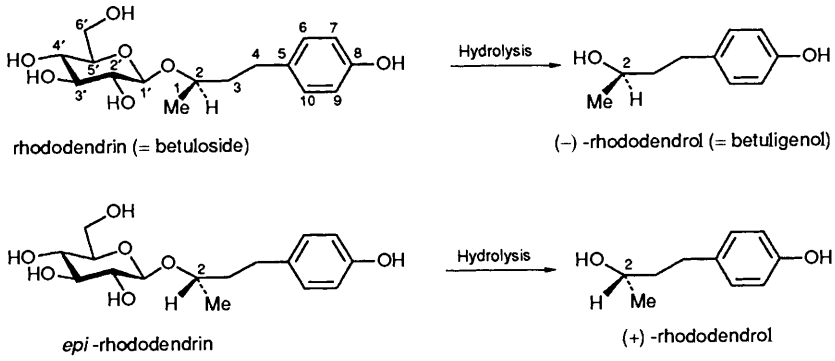
Experimental

M.p.s were determined in sulphuric acid bath and are uncorrected. UV spectra were recorded on a Beckman DU-2 spectrophotometer and the IR spectra on a Shimadzu Model 435 spectrophotometer. The NMR spectra were recorded on a JEOL JNM FX-200 FT (200 MHz) NMR spectrometer with $SiMe_4$ as the internal standard and the mass spectra were recorded on a Varian Mat 331A instrument.

Rhododendrin* was isolated from the leaves of *Taxus baccata* L. by the method of Khan *et al.*[6] and was crystallised from ethyl acetate as shining cubes; m.p. 189–191 °C; $[\alpha]_D^{21}$ −38° (*c* 0.5, water);† λ_{max}(MeOH)/nm (log ε) 220 (4.09) and 262 (3.70); +NaOMe: 236 and 289; ν_{max}(Nujol)/cm^{-1} 3340, 3220, 1615, 1600, 1515, 1315, 1285, 1240, 1162, 1100, 1080, 1055, 1035, 1005, 920 and 815; δ_H[$(CD_3)_2SO$] 1.1 (3 H, d, *J* 7, Me), 1.5–1.85 (2 H, m, 3-H_2), 2.50 (2 H, t, *J* 7, 4-H_2), 2.90–4.95 (12 H, 7 m, 2-H and sugar protons), 6.65 (2 H, d, *J* 9, 6- and 10-H), 7.00 (2 H, d, *J* 9, 7- and 9-H), and 9.05 (s, 8-OH); δ_C[$(CD_3)_2SO$] 19.52 (s, C-1), 30.02 (s, C-3), 38.87 (s, C-4), 60.02 (d, C-6′), 69.97 (d, C-4′), 72.56 (s, C-2), 73.28 (d, C-2′), 76.59 (d, C-3′), 76.71 (d, C-5′), 100.70 (s, C-1′), 114.76 (s, C-7), 114.85 (s, C-9), 129.07 (s, C-6 and -10), 132.18 (d, C-5) 155.00 (d, C-8); *m/z* (rel. intensity) 329 [(M + 1)$^+$, 0.6], 328 (M^+, 3.2), 207 ()$^+$ (2.8), 177 ()$^+$ (13), 166 (9), 149 (15), 148 (*p*-$HOC_6H_4CH_2CH$=CHMe, 31), 133 (14), 121 (11), 108 (12), 107 ()$^+$ (100), 78 (4), 77 (8), 73 (13), 60 (11), 57 (8) and 45 (7).

* The UV, IR, and detailed mass spectra of rhododendrin (betuloside) were not published earlier; it is interesting to note that our sample of the glycoside exhibits the molecular ion peak at *m/z* 328 (3%) in its mass spectrum.

† The $[\alpha]_D$-values of different samples of this glucoside isolated by different groups of workers are: −48 (*c* 1, water) for betuloside from *T. baccata*;[6] −44.3 (*c* 0.79, EtOH) for betuloside from *B. alba*;[8] −15.5 (*c* 0.1, EtOH) for *epi*-rhododendrin from *A. nikoense* MAXIM.,[21] while the respective m.p.s (°C) are: 187–190,[6] 190,[8] 192–193[14] and 81–84.[21]



Scheme 1

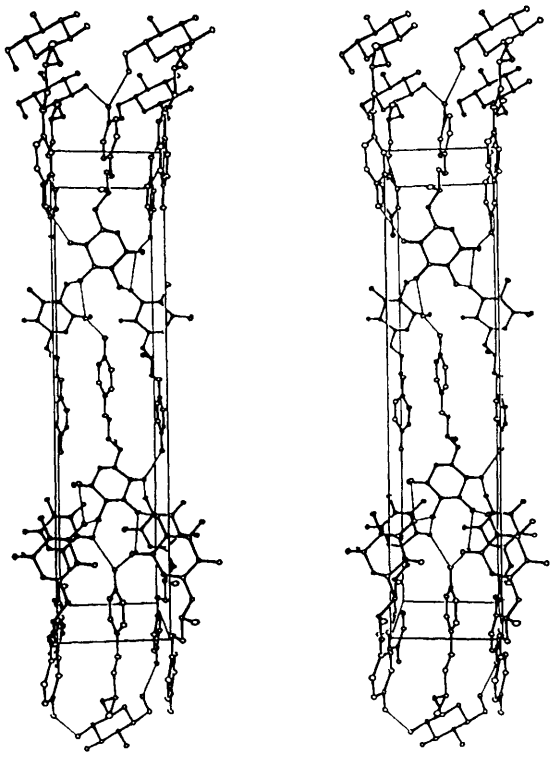


Fig. 2 Stereo-pair packing of rhododendrin

Single-crystal X-Ray Structure Determination of Rhododendrin.—A single crystal, of dimensions 0.12 × 0.22 × 0.30 mm, was selected for the X-ray analysis. The crystal was cooled to 110 K during the experiment with an Enraf–Nonius gas-flow low-temperature device. A CAD4 diffractometer was used for the data collection using Cu-Kα radiation obtained from a graphite monochromator. Rhododendrin crystallises from ethyl acetate in the orthorhombic space group $P2_12_12_1$. The setting angles for 25 reflections ($37° < \theta < 41°$) were used in a least-squares refinement to determine the unit-cell parameters: a = 6.3488(9); b = 7.6033(12); c = 33.074(5) Å; V = 1596.5(7) Å^3. The empirical formula for betuloside $C_{16}H_{24}O_7$, formula weight 328.35, gives $Z = 4$ with D_{calc} = 1.366 g cm^{-3}. The ω scan mode, $\Delta\omega = 1.6°$, was employed for the data collection, where the maximum scan time was 120 s. The intensities of three standard reflections recorded every 10 000 s remained constant throughout the experiment. Diffraction data were measured in the range $1° < \theta \leqslant 75°$. Data reduction included corrections for Lorentz and polarisation effects and symmetry-related reflections were averaged according to the symmetry of the Laue group. This gave 1943 independent reflections, 1809 of which had $|F|^2 > 2[\sigma(|F|^2) + (0.05 \times |F|^2]^2$ and were used in the structure solution and refinement. The structure was solved by application of the SHELXS-86[25] program, which gave starting co-ordinates for all the non-hydrogen atoms.

The least-squares method was used to refine the structure by minimising $\Sigma w(|F_o| - |F_c|)^2$. The positions of all the hydrogen atoms were shown clearly in a difference electron density. Only the positions of the hydrogen atoms bonded to oxygen were taken from the difference Fourier; the remaining hydrogen atoms were introduced in idealised positions. In the final refinement cycles their parameters were fixed and they were given a common isotropic displacement parameter B = 2.5 Å^2. The final residuals were R = 0.041 and R_w = 0.067. The maximum shift was 0.02 σ and the residual electron density was featureless.

Rhododendrin pentaacetate* was obtained by acetylation of rhododendrin with dry pyridine and acetic anhydride at 25 °C for 24 h and was crystallised from methanol as needles, m.p. 82–85 °C; δ_H([$^2H_6$]acetone) 1.15 (3 H, d, J 7, Me), 1.65–1.90 (2 H, m, 3-H_2), 1.95–2.10 (12 H, 4 s, 4 × OAc of sugar moiety), 2.25 (3-H, s, 8-OAc), 2.65–2.90 (2 H, m, 4-H_2), 3.80–5.35 (8 H, 7 m, 2-, 1′-, 2′-, 3′-, 4′- and 5′-H and 6′-H_2), 7.0 (2 H, d, J 9, 6- and 10-H) and 7.28 (2 H, d, J 9, 7- and 9-H); δ_C([$^2H_6$]acetone) 20.12, 20.40, 20.45, 20.50 and 20.81 (5 s, C-1 and 5 × OCO*Me*), 31.17 (s, C-3), 39.33 (s, C(4), 62.75 (s, C-6′), 69.44 (s, C-4′), 72.17 (d, C-2), 73.46, (s, C-2′), 75.26 (s, C-3′ and -5′), 99.62 (s, C-1′), 122.16 (s, C-7 and -9), 130.04 (s, C-6 and -10), 140.46 (s, C-5) and 149.85 (s, C-8) and 169.45, 169.57, 169.86, 170.16 and 170.60 (5 s, 5 × OCOMe); m/z (rel. intensity) 538 (M^+, 1), 497 (3), 496 (12), 332 (3), 331 (14), 303 (2), 229 (3), 219 (4), 191 (12), 190 (21), 169 (34), 149 (53), 148 (100), 133 (8), 115 (7), 109 (17), 107 (67), 98 (6), 81 (4) and 43 (64).

(−)-Rhododendrol was obtained by hydrolysis of rhododendrin with 5% aq. HCl by the method of Khan *et al.*[6] and was crystallised from benzene as needles, m.p. 79–80 °C; $[\alpha]_D^{21}$ −17° (*c* 0.5, MeOH);† δ_H($CDCl_3$) 1.32 (3 H, d, J 7, Me),

* The pentaacetyl derivative of this glucoside had previously been reported by Khan *et al.*,[6] the m.p. of our pentaacetate (82–85 °C) is different to that reported by them (185–186 °C).[6] The pentaacetyl derivative of rhododendrin has also been prepared by Kawaguchi *et al.*,[10] but only the m.p. (96–97 °C) was reported, which is more in line with that of our acetyl derivative. Khan *et al.*[6] have reported only ^{1}H NMR data for their derivative, while we have fully characterised our betuloside pentaacetate from its ^{1}H NMR, ^{13}C NMR, and mass spectra. It is noteworthy that in its MS the pentaacetate exhibits the molecular ion peak at m/z 538 (1%).

† The $[\alpha]_D$-values of different samples of the aglucone reported by different groups of workers are: −20 °C (*c* 1.25, EtOH) for betuligenol from *T. baccata*;[6] −18.5° (*c* 3.88, EtOH) for betuligenol from *B. alba*;[8] +20° (*c* 1.0, EtOH) for (+)-rhododendrol from *A. nikoense MAXIM.*;[21] and +17.1° (c 2.0, EtOH) for *d*-betuligenol from *R. maximum*,[20] while the respective m.p.s (°C) are: 80,[6] 81.5,[9] 81–82[14,21] and 81–83.[20]

Table 4 Protection (%) provided by rhododendrin in the levels of different enzymes in rats

Enzyme	Galactosamine model rhododendrin (10 mg kg^{-1})	Thioacetamide model rhododendrin (25 mg kg^{-1})
1 Glutamate oxaloacetate transaminase (GOT)	0	21
2 Glutamate pyruvate transaminase (GPT)	0	26
3 Acid phosphatase (ACP)	11	20
4 Alkaline phosphatase (ALP)	44	36
5 Glutamate dehydrogenase (GDH)	1	100

1.57 (br s, 2-OH), 1.67–1.85 (2 H, m, 3-H_2), 2.52–2.77 (2 H, m, 4-H_2), 3.75–3.92 (1 H, m, 2-H), 5.40 (br s, 8-OH), 6.75 (2 H, d, *J* 9, 7- and 9-H) and 7.05 (2 H, d, *J* 9, 6- and 10-H); $\delta_C(CDCl_3)$ 23.43 (s, C-1), 31.09 (s, C-3), 40.87 (s, C-4), 67.63 (s, C-2), 115.20 (s, C-7 and -9), 129.32 (s, C-6 and -10), 133.82 (s, C-5) and 153.74 (s, C-8); *m/z* (rel. intensity) 167 [$(M + 1)^+$, 4], 166 (M^+, 36), 149 (4), 148 (26), 134 (8), 133 (76), 121 (6), 120 (6), 108 (19), 107 (100), 105 (4), 103 (4), 94 (14), 91 (10), 78 (6), 77 (22), 65 (6), 55 (5), 45 (19), 43 (8) and 39 (10).

Hepatobiliary Effect of Rhododendrin.—For both the experiments, male Sprague-Dawley rats (100–125 g) were caged separately in groups of five animals each. Group I consisted of normal animals. Group II animals were administered the hepatotoxin galactosamine hydrochloride (800 mg kg^{-1}, i.p. × 1) or thioacetamide (200 mg kg^{-1}, s.c. × 1). Group III animals were fed the respective doses of rhododendrin and were injected with the hepatotoxin on day 7.

Animals of all three groups were sacrificed 24 h after administration of the hepatotoxin and their blood was collected and subjected to centrifugation (Remi C-23 cooling centrifuge) at 2000 rpm for 0.2 h. In the serum, different enzymatic parameters as described in Table 4 were analysed according to standard laboratory methods. The hepatoprotective activity of the drug was assessed by the percentage reversal effected by the drug on various enzyme levels elevated by the hepatotoxin.

Acknowledgements

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References

1 Part of this work was presented at the 17th IUPAC International Symposium on the Chemistry of Natural Products held in New Delhi (India), 4th–9th Feb., 1990.
2 R. W. Miller, R. G. Powell, C. R. Smith, Jr., E. Arnold and J. Clardy, *J. Org. Chem.*, 1981, **46**, 1469.
3 R. N. Chopra, S. L. Nayar and I. C. Chopra, *Glossary of Indian Medicinal Plants*, CSIR, New Delhi, 1956, p. 240.
4 S. B. Vohora and I. Kumar, *Planta Med.*, 1971, **2**, 100.
5 G. Chauviere, D. Guenard, C. Pascard, F. Picot, P. Potier and T. Prange, *J. Chem. Soc., Chem. Commun.*, 1982, 495.
6 M. S. Y. Khan, I. Kumar, J. S. Prasad, G. R. Nagarajan, M. R. Parathasarathy and H. G. Krishnamurty, *Planta Med.*, 1976, **30**, 82.
7 K. Archangelsky, *Arch. Exp., Pathol. Pharmakol.*, 1901, **46**, 313.
8 A. Sosa, *C. R. Hebd. Séances Acad. Sci.*, 1933, **196**, 1827.
9 A. Sosa, *Ann. Chim. (Paris)*, 1940, **14**, 5.
10 R. Kawaguchi, K. G. Kim and H. K. Kim, *J. Pharm. Soc. Jpn.*, 1942, **62**, 4 (*Chem. Abstr.*, 1950, **44**, 9634).
11 K. U. Kim, *J. Pharm. Soc. Jpn.*, 1943, **63**, 103 (*Chem. Abstr.*, 1951, **45**, 4222).
12 H. Thieme and H. J. Winkler, *Pharmazie*, 1969, **24**, 703; H. Thieme, E. Walewska and H. J. Winkler, *Pharmazie*, 1969, **24**, 648.
13 J. B. Harborne and C. A. Williams, *Phytochemistry*, 1971, **10**, 2727.
14 T. Kurihara, M. Kikuchi, S. Suzuki and E. Toyoda, *J. Pharm. Soc. Jpn.*, 1976, **96**, 1407 (*Chem. Abstr.*, 1977, **86**, 117585).
15 F. S. Santamour, Jr. and H. E. Vettel, *Biochem. Syst. Ecol.*, 1978, **6**, 107 (*Chem. Abstr.*, 1978, **89**, 176310).
16 T. Chakrabortty, A. Nandt, G. Poddar and J. S. Pyrek, *Fitoterapia*, 1987, **58**, 56 (*Chem. Abstr.*, 1987, **107**, 233061).
17 O. D. Barnaulov, A. Y. Limarenko, V. A. Kurkin, G. G. Zapesochnaya and A. N. Shchalinskii, *Khim. Farm. Zh.*, 1986, **20**, 1107 (*Chem. Abstr.*, 1987, **106**, 60790).
18 M. Klischies and M. H. Zenk, *Phytochemistry*, 1978, **17**, 1281.
19 G. F. Van Rooyen, M. J. Pietersee and C. v. d. M. Brink, *J. S. Afr. Chem. Inst.*, 1967, **20**, 54.
20 W. H. Tallent, *J. Org. Chem.*, 1964, **29**, 988.
21 T. Inoue, Y. Ishidate, M. Fujita, M. Kubo, M. Fukushima and M. Nagai, *J. Pharm. Soc. Jpn.*, 1978, **98**, 41 (*Chem. Abstr.*, 1978, **88**, 133254).
22 M. Kubo, M. Nagai and T. Inoue, *Chem. Pharm. Bull.*, 1983, **31**, 1917.
23 E. Hough, S. Neidle, D. Rogers and P. G. H. Troughton, *Acta Crystallogr., Sect. B*, 1973, **29**, 365.
24 G. M. Brown and H. A. Levy, *Acta Crystallogr., Sect. B*, 1979, **35**, 656.
25 G. M. Sheldrick, SHELXS-86. Program for Crystal Structure Determinations, University of Gottingen, Federal Republic of Germany, 1986.

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