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Flavonol Glycosides from the Leaves of *Zizyphus jujuba*

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Abstract—From the leaves of *Zizyphus jujuba* (Rhamnaceae), rutin and isoquercitrin were isolated and characterized by chemical and spectral analysis.

Keywords—*Zizyphus jujuba* · Rhamnaceae · flavonol glycosides · rutin · isoquercitrin

The seeds of *Zizyphus jujuba* (Rhamnaceae) have been used in traditional medicine for treating insomnia and nervous debility. In earlier publications, we described the isolation and structure determination of new flavone-C-glycosides[1-3] as its sedative principles. Although there is no report on folkloric uses of the leaves, a phytochemical investigation on this plant part was initiated to seek a source of flavone-C-glycosides.

Crystallization of the flavonoid fraction from MeOH extract gave compound I, mp 186~8°, as a major compound. The mother liquor was chromatographed to afford the second compound II, mp 236~8°. Both compounds showed characteristic color reactions and IR spectral properties for flavonol glycosides. The UV spectral responses to shift reagents of both compounds showed the presence of four free hydroxyls at 5, 7, 3′, 4′-positions with 3-hydroxyl substituted[4]. Acid hydrolysis of each compound afforded quercetin(III), mp 310-2°, as the genin and glucose and rhamnose from compound I and glucose only from II, respectively.

The NMR spectra of both compounds supported the above formulations. It showed that the sugar unit in each compound is attached at C-3 of quercetin and that in compound I, the signal for the anomeric proton of rhamnose was found at 4.52ppm[4] indicating that rhamnose is linked to glucose rather than to the genin. The NMR spectrum of peracetate of compound I showed that ratio of the integration of region 4.5~5.5 ppm to that of 3.2~3.8 ppm was 8:4. This observation supported that the disaccharide of compound I is rutinose[5]. Therefore the structures of compound I and II were established as rutin and isoquercitrin which were finally identified by direct comparison with authentic samples. No flavone-C-glycosides were detected but saponins(jujubosides) were detected in saponin fraction from this plant part. This is first reported isolation of both flavonoids from this plant.

Experimental

Plant material—The leaves(125g) of *Zizyphus jujuba* were collected near Seoul in summer, 1982.

Fractionation and isolation—The leaves were extracted with MeOH to give 37g of MeOH extract which was then partitioned with $CHCl_3$ and H_2O. The H_2O soluble portion was subsequently partitioned with BuOH to give BuOH soluble(8.6g) and H_2O soluble(13.2g) subfractions. The BuOH soluble subfraction was

washed with 5% KOH solution to divide into saponin fraction(2.1g) and flavonoid fraction (6.3g). The flavonoid fraction was crystallized from MeOH to yield compound I. The mother liquor was chromatographed first over SiO_2 ($CHCl_3$-MeOH-H_2O=520:280:80) and subsequently over Sephadex LH-20(MeOH) to afford compound II.

Compound I—I was crystallized from MeOH to give yellowish rosettes(0.57%). mp 186-8°, $[\alpha]_D^{20}$+0.9° (c, 0.53 in MeOH). ir, νmax (KBr) 3420 (OH), 1653(α,β-unsaturated C=O), 1598, 1569, 1500, 1455 (C=C), 1085, 1059 and 1007 cm^{-1}(C-O). uv, λmax(MeOH) 257.5 nm(log ε 4.51), 267(sh, 4.46), 306(sh, 4.14), 385.5(4.44); λmax(CH_3ONa) 273(4.59), 329.5 (4.18), 410.5(4.59); λmax($AlCl_3$) 275.5(4.59), 305(sh, 4.04), 339(3.88), 434(4.58); λmax ($AlCl_3$+HCl) 275(4.52), 300(4.11), 364.5(sh, 4.31), 404(4.39); λmax(H_3BO_3+NaOAc) 262 (4.59), 297(4.05), 379.5(4.48); λmax(NaOAc) 274(4.54), 325.5(4.23), 379(4.37).

H^1-nmr (80MHz, CD_3OD)δ 1.11(3H, d, *J*=5.5Hz, rha-CH_3), 4.52(1H, s, rha H-1), 5.08 (1H, d, *J*=6.5Hz, glu H-1), 6.21(1H, d, *J*=2Hz, H-6), 6.40(1H, d, *J*=2Hz, H-8), 6.84 (1H, d, *J*=9Hz, H-5′), 7.58(1H, dd, *J*=2 and 9Hz, H-6′), 7.62(1H, d, *J*=2Hz, H-2′).

Compound II—II was crystallized from MeOH to yield yellowish needles(0.056%). mp 236-8°, $[\alpha]_D^{20}$ −8° (c, 0.25 in MeOH). ir, νmax(KBr) 3350, 3180(OH), 1655(α,β-unsaturated C=O), 1602, 1556, 1459, 1445(C=C), 1070, 1053 and 1005cm^{-1}(C-O). uv, λmax(MeOH) 258nm(log ε 4.23), 268(sh, 4.17), 303(sh, 3.85), 359(4.05); λmax(CH_3ONa) 273(4.33), 330.5(3.93), 412(4.29); λmax($AlCl_3$) 276(4.31), 305(sh, 3.76), 335(3.59), 435(4.31); λmax ($AlCl_3$+HCl) 271(4.24), 301(3.81), 364(sh, 4.02), 404(4.11); λmax(H_3BO_3+NaOAc) 262 (4.32), 297(3.78), 380(4.22); λmax(NaOAc) 275(4.27), 326.5(3.96), 376(4.09).

H^1-nmr (80MHz, DMSO-d_6)δ 5.47(1H, bs, glu H-1), 6.21(1H, d, *J*=2Hz, H-6), 6.41(1 H, d, *J*=2Hz, H-8), 6.85(1H, d, *J*=8Hz, H-5′), 7.58(1H, dd, *J*=2 and 8Hz, H-6′), 7.63 (1H, d, *J*=2Hz, H-2′), 12.62(1H, bs, 5-OH).

Acid hydrolysis of compound I and II—Hydrolysis of compound I(30mg) and II(15mg), separately, with 5% H_2SO_4 in dioxane-H_2O (1:1) under reflux for 3hr was followed by the usual work-up.

Crystallization of the each aglycone from MeOH yielded the same quercetin(III), mp 310-2°, which was confirmed by comparison with an authentic sample(tlc, mmp, uv). The filtrate was separately neutralized with $BaCO_3$, filtered and concentrated. d-glucose and l-rhamnose from compound I and d-glucose from compound II were identified by tlc(precoated cellulose, pyridine-EtOAc-HOAc-H_2O=36:36:7:21; Rf 0.27 for glucose and 0.57 for rhamnose).

Acetylation of compound I—A sample(20 mg) of I was acetylated with Ac_2O/pyridine (1ml each) at room temperature overnight. The reaction mixture was followed by the usual work-up.

H^1-nmr (80MHz, $CDCl_3$)δ 1.05(3H, d, *J*=6.2 Hz, rha-CH_3), 1.93(3H, s, OAc), 1.94(3H, s, OAc), 2.02(6H, s, 2×OAc), 2.08(3H, s, OAc), 2.13(3H, s, OAc), 2.29(3H, s, OAc), 2.33(6H, s, 2×OAc), 2.44(3H, s, OAc), 3.2-3.8(4H, glu H-5, 6 and rha H-5), 4.5-5.5(8H, rha H-1, 2, 3, 4 and glu-1, 2, 3, 4), 6.79(1H, d, *J*=2.3 Hz, H-6), 7.24(1H, d, *J*=2.3Hz, H-8), 7.32 (1H, d, *J*=7.7Hz, H-5′), 7.87(1H, d, *J*=2.1 Hz, H-2′), 7.92(1H, dd, *J*=7.7 and 2.1Hz, H-6′).

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