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Reduction of Sweetness Judgements by Extracts from the Leaves of *Ziziphus jujuba*[1]

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MEISELMAN, H. L., B. P. HALPERN AND G. P. DATEO. *Reduction of sweetness judgments by extracts from the leaves of* Ziziphus jujuba. PHYSIOL. BEHAV. 17(2) 313–317, 1976. – Human judgments of the sweetness of sucrose solutions were significantly reduced by an aqueous-alcohol extract from the leaves of the rhamnaced tree, *Ziziphus jujuba,* but were not changed in quality category. Both water soluble and water insoluble portions were taste-active. Fractionation of the water soluble portion of the extract by solvent partition yielded an active fraction with saponin properties. *Ziziphus jujuba* contains a taste modifier which can be used as a tool in taste research.

Taste intensity Taste Taste alteration *Ziziphus jujuba* Sucrose *Gymnema sylvestre*

SEVERAL natural substances of plant origin modify the sense of taste by selectively changing the characteristics of gustatory receptors and/or primary neurons. Two widely studied substances are miraculin, a protein, [9, 19, 22] and gymnemic acid, a triterpene saponin [1, 10, 17, 21]. Such peripheral gustatory modifiers can be employed in theoretically oriented studies of taste neurophysiology [1, 9, 10, 17, 19, 21, 22] and psychophysics [3, 4, 25], in examinations of plant–animal interaction [11, 13, 23, 26, 27], and perhaps, in modifications of human food acceptability [2, 6, 35]. The action of gustatory modifiers can be primarily an alteration of classes or quality categories of the responses or primarily a depression or enhancement of the intensity of otherwise unchanged quality categories. In either case, one, or more than one, quality category may be affected. Miraculin, an extract from the ripe fruit of the shrub *Synsepalum dulcificum,* is a specific modifier. Miraculin produces a modification of judgments of those acidic substances which are typically judged sour by humans before treatment, and sweet after treatment [3]. Preparations of gymnemic acid, another frequently studied taste modifier, produce, in humans, alterations of both quality category and response intensity for the tastes of sugars, alkaloids, and amino acids (for references see [4,28]. We now report a taste modification produced in humans by extracts from the leaves of the jujube tree, *Ziziphus jujuba.*

Z. jujuba [7, 18, 31, 32] is cultivated in the Middle and Far East and has grown in Mediterranean countries and Southern Europe for 2,000 years. It was introduced into the United States in 1837. The fruits of the tree are edible, while the leaves are said to be used in Iran to decrease the intake of sweets [15].

Giordano [15] and Kohlberg [24] have both reported that leaf extracts of *Z. jujuba* elevate human taste thresholds to sucrose solutions. Both used a technique to determine the concentration of sucrose solution discriminated from water (detection threshold) and the concentration of sucrose solution discriminated from water as sweet (recognition threshold). For both types of threshold, the psychophysical task consisted of the ascending and descending method of limits (successively increasing or decreasing stimulus concentrations) [12]. Each stimulus presentation followed a triangle test format, composed of single drops of sucrose solution or distilled water.

Giordano demonstrated, in one subject tested repeatedly, that either directly chewing the leaves of *Z. jujuba* or rinsing with a water extract produced a doubling of the recognition and detection thresholds for sucrose. Two tests in the same subject yielded no change in thresholds for sodium chloride. Kohlberg reported that 200 mg of leaves chewed for 2 min abolished the sweetness of a 200 mM sucrose solution for 3 min (as compared with 15 min for

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Gymnema sylvestre). Using the ethanol soluble fraction of a water extract of the leaves, Kohlberg also reported a two fold increase in the recognition threshold for sucrose sweetness but no abolition of the taste. As little as 100 mg of active crude anti-sweet principle ("onnabin") abolished the sweetness of 200 mM sucrose. Kohlberg further reported that the anti-sweet effect also worked on 10 mM cyclamate, 0.33 mM saccharin, and 822 mM glycerol.

Halpern and Singer-Granich (unpublished observations) studied the effect of *Z. jujuba* on taste intensity judged by 8 subjects chosen for consistency of naming taste solutions and of estimating stimulus strengths. An aqueous decoction of *Z. jujuba* leaves (10 g/100 ml H_2O) was held in the mouth for 3 min followed by a series of presentations of 80 mM sucrose, separated by the series: 10 sec–10 sec rinse–10 sec rest. Whereas a quinine control did not affect estimates of sucrose strength, the *Z. jujuba* extract reduced sweetness almost 90% on the average with a return to near original sweetness by the end of the last of 10 trials (5 min). These results provide more quantitative information about the reduction of sweetness by *Z. jujuba* and confirm the earlier observation that its time course is of shorter duration than that of *Gymnema sylvestre.*

The present study assessed the effects of *Z. jujuba* with a set of taste stimulus solutions psychophysically matched for judged intensities at relatively high and low concentrations (matched to 300 mM or 75 mM NaCl). The effect of a *Z. jujuba* extract on repsonses to these solutions was measured using judgements of quality categories and judged intensity.

METHOD

Subjects

The 8 male and 2 female volunteers were technicians at U.S. Army Natick Development Center, ages 21–26 years. They were experienced in magnitude estimations of taste stimuli, but not aware of the specific purpose of the present experiment.

Stimuli

Z. jujuba leaves were picked in October 1972, from a 54 year old cluster of *Z. jujuba* trees in the arboretum of Highland Park, Monroe County Department of Parks, Rochester, NY. The leaves were dried by an air stream (30°C) and stored at 5°C over silica desiccant. An aqueous alcohol extract of the leaves was obtained by the procedure of Dateo and Long [8]. The combined extract (517 ml) from 25 g of dried leaves was concentrated in vacuum at subambient temperature. Precipitated material was separated by centrifugation (30,000 rpm). The aqueous supernatant (60 ml) was diluted to 100 ml with ethanol, and the water insoluble precipitate (insoluble in ethanol) dissolved in 50% ethanol (ea 100 ml). To facilitate testing of water insoluble materials, microcrystalline cellulose powder (Cellex MX, Bio-Rad) was used to disperse the sample. A solution of the water insoluble portion of the aqueous alcohol extract was absorbed on the powder. The wet powder was air dried at 40°C and then vacuum dried at room temperature (silica desiccant). Before use, the absorbed extracts (250 mg of powder/ml) were dispersed in water. Acidity was monitored by pH paper and not found to deviate from the pH range 5–6.

To test the hypothesis that the active principle of *Z. jujuba* was gymnemic acid, the total concentrate of an aqueous alcohol extract was partitioned into hexane soluble, ether soluble, chloroform ethanol soluble and aqueous residue [8]. The chloroform-ethanol fraction was analyzed by thin layer chromatography for gymnemic acid. Figure 1 depicts the results. Gymnemic acid was not detected. The appearance of components visualized by a Liebermann-Burchard reagent and the foaming properties of the chloroform-ethanol fraction in water suggest that saponins are present in the active fraction.

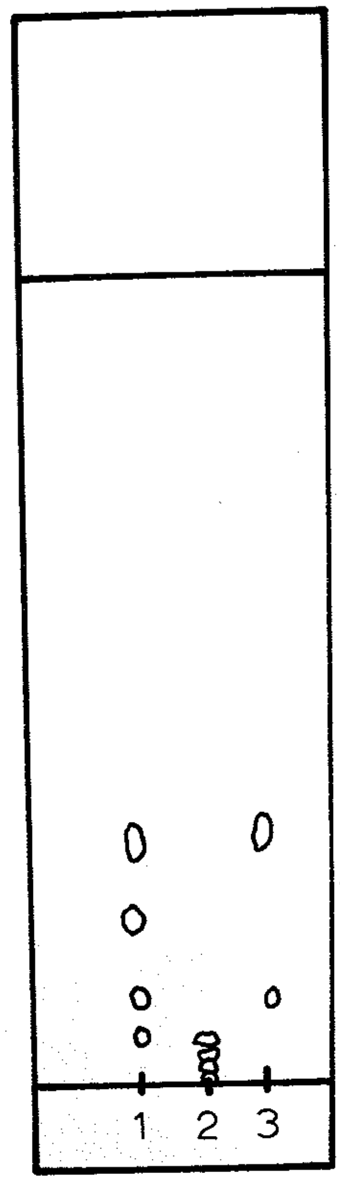

FIG. 1. Schematic of a thin layer chromatogram of the chloroform-ethanol soluble fraction of *Z. jujuba* leaves. Ascending development on silica gel G with the solvent system III: butyl formate–methyl ethyl ketone–formic acid–water [8]. 1. gymnemic acid A [34]. 2. *Z. jujuba* fraction. 3. Chloroform-ethanol fraction from *G. Sylvestre.* The most mobile spot is gymnemic acid A_1. The coloration obtained with Liebermann-Burchard spray reagent from the *Z. jujuba* components differs from that found with gymnemic acid spots.

Hexane soluble and ether soluble fractions were absorbed on microcrystalline cellulose. The chloroform-ethanol soluble fraction was dissolved in water (1% w/v), washed with ether and lyophilized. Lyophilized aqueous residue was also absorbed from aqueous ethanol on microcrystalline cellulose.

Taste stimuli for testing the extract were aqueous solutions of reagent grade NaCl, HCl, sucrose, and U.S.P. quinine hydrochloride (QHCl). The solvent for all taste solutions (and the rinse liquid, per se) was distilled water (refractive index = 1.3330, 20°C). Two sets of taste stimulus solutions were used, one psychophysically matched to 300 mM NaCl (high concentration) and the other matched to 75 mM NaCl (low concentration).

Procedure

In each session, subjects held 10 ml dispersion of leaf extract in their mouths for 3 min, expectorated, waited 30 sec, rinsed with distilled water, sipped 10 ml of one concentration of a taste stimulus, held it in their mouths for 3 sec, expectorated, and then judged the intensity and reported the quality category.

Magnitude estimates were done according to the method of Stevens [33]. The 75 mM or 300 mM NaCl standard solution was assigned a magnitude rating of 10, and the strengths of all other stimuli in that session were judged in proportion to that standard. If a solution was judged to taste twice as strong, it was assigned the number 20 and so on. Quality category reports were restricted to salty, sour, sweet, or bitter.

Six sessions were conducted. In the first 2, water soluble and water insoluble portions of the aqueous alcohol extract were tested on high and low concentrations of the test stimuli. In the second four sessions, conducted on two separate days, the four *Z. jujuba* fractions prepared from the water soluble portion of the aqueous alcohol extract were tested. The order of conditions within the first two sessions, and the last four sessions were randomized.

RESULTS

Both alcohol soluble and water insoluble portions of *Z. jujuba* extracts significantly depressed the judged intensity of high and low concentrations of sucrose (Table 1). There were no significant changes in the judged intensity of the other taste solutions (Table 1). A change in reported quality occurred for only 1 subject, on 1 trial. Other than this, all subjects called NaCl salty, HCl sour, sucrose sweet, and QHCl bitter. Thus, *Z. jujuba* produced only a reduction in the judged intensity of sweetness.

With the 4 fractions of the water soluble portion of the aqueous alcohol extract, the ether soluble, and chloroform-ethanol soluble fractions significantly depressed sweetness judgements of the sucrose solutions, but did not alter the qualitative category (Table 2). The other 2 fractions, hexane soluble and aqueous residue, had no significant effects on the sucrose taste solutions. All 4 fractions yielded a significant enhancement of sourness (Table 2).

DISCUSSION

A reduction in the judged sweetness of sucrose solutions was produced by portions of the aqueous-alcohol extracts of *Z. jujuba* leaves. The 2 inactive fractions of solvent partition (i.e. the hexane soluble and aqueous residue) provide, in effect, control solutions. Because the enhancement of sourness occurred for all 4 fractions of the aqueous-alcohol extract, whereas the sweetness reduction occurred only for the ether and chloroform-ethanol soluble fractions, sourness enhancement appears to be independent of the sweetness reduction action of *Z. jujuba*. Therefore, this fractionation experiment indicates that: a) The general psychophysical procedure of this study does not necessarily lead to changes in the judged intensity of a sucrose solution. b) Some fractions of the aqueous-alcohol extract of *Z. jujuba* leaves cause no changes in sweetness judgments. c) The positive results were produced using 2 fractions with specific partition (i.e., physicochemical) characteristics, the ether soluble and chloroform-soluble fraction.

TABLE 1

MEAN MAGNITUDE ESTIMATES OF TASTE SOLUTION (NaCl STANDARDS=10) JUDGED INTENSITY AFTER APPLICATION TO THE TONGUE OF WATER SOLUBLE OR WATER INSOLUBLE PORTIONS OF AN AQUEOUS ALCOHOL EXTRACT OF *Z. JUJUBA*. THE WATER SOLUBLE EXTRACT WAS A MICROCRYSTALLINE CELLULOSE DISPERSION OF 33 mg, EQUIVALENT TO THE WATER SOLUBLE PROTION FROM 100 mg OF LEAF MATERIAL. THE WATER INSOUBLE WAS A DISPERSION OF 11 mg, EQUIVALENT TO THE YIELD FROM 120 mg OF LEAF

Taste Solutions	Portion: Water Soluble	Water Insoluble
	High Concentrations	
300 mM NaCl	11.5	11.7
6 mM HCl	12.9	13.7
0.2 mM QHCl	12.2	10.2
400 mM Sucrose	5.9*	6.1*
	Low Concentrations	
75 mM NaCl	12.5	11.6
2.6 mM HCl	12.3	12.3
0.034 mM QHCl	12.3	11.9
100 mM Sucrose	6.6*	8.6*

*Analysis of variance, F test, $p<0.001$; Duncan's multiple range tests, $p<0.01$ only for comparisons of other stimuli with sucrose, all other comparisons, $p>0.05$.

TABLE 2

EFFECT OF *Z. JUJUBA* FRACTIONS ON MEAN MAGNITUDE ESTIMATES OF TASTE SOLUTION INTENSITY. NaCl SOLUTION WAS INTENSITY STANDARD (=10). FRACTIONS WERE OBTAINED BY PARTITION BETWEEN SOLVENT AND THE AQUEOUS CONCENTRATE OF AN AQUEOUS-ALCOHOL EXTRACT. THE WEIGHTS OF FRACTIONS/LEAVES WERE: HEXANE, 27 mg/2.5 g; ETHER, 32 mg/6.5 g; $CHCl_3$-ETHANOL, 30 mg/2.0 g. WATER (RESIDUE) 30 mg/90 mg ORIGINAL EXTRACT

Taste Solution			Fraction: Hexane Soluble	Ether Soluble	$CHCl_3$-Ethanol Soluble	Aqueous Residue
NaCl	75	mM	9.3	13.0	9.0	11.1
HCl	2.6	mM	12.8†	14.7†	12.4†	14.5†
QHCl	0.034	mM	11.6	11.8	8.0	9.9
Sucrose	100	mM	10.6	5.5*	5.6*	10.7

*,†Analysis of variance, F test, $p<.001$. Duncan's multiple range test, $p<0.01$(†) or $p<0.05$(*).

The activity of the water insoluble portion of the extract may be attributable (if one assumes the active principle itself is a saponin) to alkaline earth salts of the active material or some water insoluble complex that can be solubilized by the action of saliva. The presence of active principle in both ether soluble and chloroform-ethanol soluble fractions is similar to the observation of Stoecklin, Weiss, and Reichstein [34]. They found that ether soluble and chloroform-ethanol soluble fractions from *Gymnema sylvestre* leaves have antisaccharine activity, and suggested that this may be due to some extraction by ether of material to be found mainly in the chloroform-ethanol soluble fraction.

Despite the common characteristic of both being saponins, the sweet-reducing principle from the leaves of *Z. jujuba,* which we designate "ziziphin", differs from gymnemic acid chemically, ecologically, and psychophysically. From the chemical point of view, a comparison using thin layer chromatography (TLC) demonstrates that the migration patterns of gymnemic acid and ziziphin are quite different (Fig. 1). Therefore, no activity corresponding to gymnemic acid is present in the *Z. jujuba.*

Ecologically, the degree of insect predation upon *Z. jujuba* and *G. sylvestre* can be compared. *Z. jujuba* leaves are attacked by many insects in India, including 33 families in 6 different orders [27], and by one common pest, *Popilla japonica* (Japanese bettle) in the United States (Vogt, personnal communication). This indicates that the intact leaf and probably ziziphin is neither a feeding deterrent, a taste modifier, nor toxic to these insects. In contrast, pure gymnemic acid is a feeding deterrent for a broadly phytophageous insect, the southern army worm [16]. Further, only one species of insect (the uraniid lepidoptera *Micronia aculeta*) is known to attack the leaves of *G. sylvestre* [26]. These ecological data are consistent with the preceding chemical data which indicated that gymnemic acid and ziziphin differ in physicochemical properties.

Further psychophysical observations are needed to confirm any distinction between gymnemic acid and ziziphin. The present experiment suggests an effect of ziziphin only on sweetness judgements. However, the previous studies of gymnemic acid have observed effects other than sweetness reduction with complex stimuli [28]. Future studies with ziziphin should explore its effects on complex stimuli with special emphasis on potential sour enhancement, and temporal parameters. Thus, chemical and ecological factors establish a distinction between ziziphin and gymnemic acid. Additional psychophysical data are needed to establish the ways in which their effects on humans might differ.

A different but interesting observation is the effectiveness of the water insoluble portion of the aqueous alcohol extract of *Z. jujuba* leaves. It is usually stated that only water soluble substances can have taste effects [5,30]. However, several considerations must be made. First, insoluble is a relative term. It indicates that a substance does not readily go into solution in a particular solvent system. So-called insoluble (in water) substances which are nonetheless effective taste stimuli (in aqueous solutions) have been described [14]. In the case of our insoluble portion of the aqueous-alcohol extract of *Z. jujuba,* neither pure water, nor pure ethanol were good solvents. Psychophysical testing using the original aqueous alcohol extract was not done because of the direct effect of ethanol on taste responses [20]. The cellulose absorption technique permitted us to deliver both soluble and insoluble portions inside the mouth in the same manner. Since the water insoluble portion was taste-active, the component absorbed on the cellulose is sufficiently soluble in saliva and/or the surface of the membrane of taste receptors to reach an effective concentration.

The identification of ziziphin as a taste modifier which produces a brief and reversable alteration in the sweetness of sucrose produces a new, important tool for gustatory research. Further chemical studies are required to characterize ziziphin, psychophysical studies are required to adequately define an appropriate range of taste stimuli, and behavioral and electrophysical investigations of the type performed with other taste modifiers are required to verify the locus of action and indicate the effects of ziziphin on taste in non-human species. A wide geographic distribution of the tree both provides abundant supplies of the leaves and encourages ecological studies of predators of this significant research tool.

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