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Evaluation of Bitter Masking Flavanones from Herba Santa (*Eriodictyon californicum* (H. & A.) Torr., Hydrophyllaceae)

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Products made from Herba Santa (*Eriodictyon californicum* (H. & A.) Torr.) have been used as bitter remedies for some pharmaceutical applications for many years, but they are actually too aromatic to be useful for many food or pharmaceutical applications. In sensory studies flavanones homoeriodictyol (**1**), its sodium salt (**1-Na**), sterubin (**2**), and eriodictyol (**4**) could significantly decrease the bitter taste of caffeine without exhibiting intrinsic strong flavors or taste characteristics. Further investigations on **1-Na** elicited a broad masking activity between 10 and 40% toward different chemical classes of bitter molecules (e.g. salicin, amarogentin, paracetamol, quinine) but not toward bitter linoleic acid emulsions. For caffeine and amarogentin, dose−response studies were performed; the masking activity toward bitter taste for both compounds reached a plateau at higher concentrations of **1-Na**. Due to these facts, homoeriodictyol sodium salt (**1-Na**) seems to be a very interesting new taste modifier for food applications and pharmaceuticals.

KEYWORDS: Bitter masking; flavanones; taste modifiers; homoeriodictyol; eriodictyol; Herba Santa

INTRODUCTION

Pronounced bitter taste of some foodstuffs is tolerated or even desired in only a few cases, e.g. in coffee, tea, or bitter lemon. Mostly, the compounds which are responsible for the bitter, astringent, or harsh taste are either eliminated from raw materials and foodstuffs or masked by sodium chloride, acids, and/or sugar (*1*). Unfortunately, a lot of the potential beneficial phytonutrients, such as polyphenolic acid derivatives, flavonoids, isoflavones, terpenes, and glucosinolates, are described as bitter, astringent, or acrid, as reviewed by Drewnowski and Gomez-Carneros (*2*). As a consequence, it was proposed that the avoidance of bitter legumes or fruits at least by supertasters may contribute to the increased risk of suffering from cardiovascular diseases, obesity, or diabetes (*3*, *4*).

A lot of different methods were developed to diminish the bitter tasting compounds in raw materials and finished products: breeding of plants to obtain less bitter varieties; optimization of fermentation of milk and other protein-containing raw materials (*5*); debittering of citrus, especially orange and grapefruit juices by precipitation or enzymatic degradation of naringin (*1*). A simple way to mask bitterness is to add sugar or other sweeteners, e.g. neohesperidine dihydrochalcone (*6*), but it fails for nonsweet applications. In some cases, the addition of proteins, e.g. milk in coffee or tea, may debitter the products, but other taste and aroma qualities are altered significantly, too. Simple sodium salts in a concentration range from 0.1 to 0.5 mol L^{-1} (i.e. 0.5−2.5% NaCl) are able to reduce the bitter taste of many bitter compounds (*7*), and this approach has been used in food preparation since ancient times. But high sodium intake is correlated to higher blood pressure, and for health reasons the salt consumption should be limited (*8*). Some recently suggested solutions for the bitter problem were the use of Lactisole (2-(4-methoxyphenyloxy)propionic acid) (*9*, but cf. ref. *10* on contrary results) and of nucleotides such as AMP (*11*). The nucleotides were assumed as acting directly on the bitter receptors expressed on taste cells.

In the late 19th century alcoholic liquid extracts of Herba Santa were suggested as bitter masking agents (*12*) for quinine. Herba Santa (or Yerba Santa, holy weed, bears weed, mountain balm) is the common name of the chaparall shrub *Eriodictyon californicum* (H. & A.) Torr. (Hydrophyllaceae) which is widely distributed in central and northern California coastal ranges, northern Baja California, Sierra Nevada, and the southern Oregon mountains (*13*). The plant and its preparations have been used by American Indians since ancient times, e.g. against cold and asthma (*14*). In earlier studies it was shown that the most important single constituents of the plant dry material are flavonoids, especially the flavanones homoeriodictyol (**1**), 7-methyleriodictyol (**2**, sterubin), and hesperitin (**3**); minor flavonoids are eriodictyol (**4**), chrysoeriol (**5**), and luteolin (**6**) (for structures, cf. **Figure 1**). The flavanones are mainly located in the leaf wax (*13*).

A study performed in 1933 stated that eridodictyol (**4**) and homoeriodictyol (**1**) were not the active principles which were able to mask quinine (*15*). The authors suggested that only the "whole resins" of Herba Santa were active by adsorbing the

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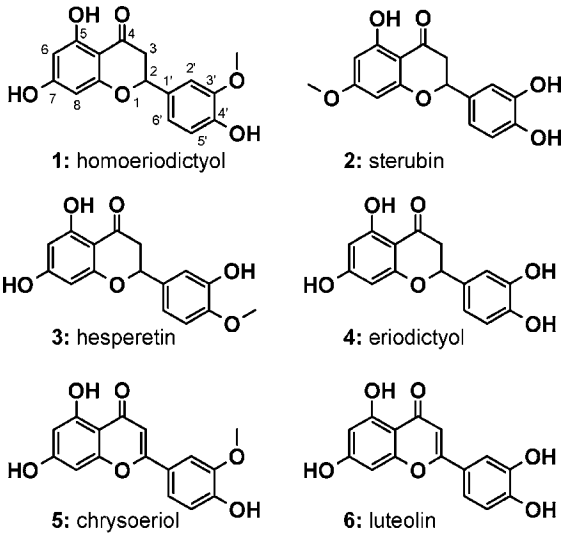

Figure 1. Most important flavonoids from *Eriodictyon californicum* (H. & A.) Torr. The flavanones are located mainly in the leaf waxes.

evaluated alkaloids quinine, strychnine, and codeine. Since then no further research regarding the bitter masking activity of Herba Santa has been published. Some other studies on occurrence and functions of flavanones from *Eriodictyon ssp.* were described (e.g. against cancer (*16*)). Bacon et al. determined the level of flavanones in several varieties of Herba Santa (*17*): homoeriodictyol (**1**) occurs only in *E. californicum* (H. & A.) Torr. and *E. angustifolium* Nutt. but not in *E. tormentosum* Benth. The UV spectrum of homoeriodictyol shows λ_{max} at 290 and at 320−340 nm, and it was suggested that these flavanones were produced as protectants against UV-light-induced damages of plant tissues (*13*).

Because products made from Herba Santa are in fact used as bitter remedies for some pharmaceutical applications but are too aromatic themselves to be useful for many food or pharmaceutical applications, we have performed a bioguided fractionation of plant constituents and evaluated the most active principles for their masking properties in depth.

MATERIALS AND METHODS

Authentic samples of homoeriodictyol and eriodictyol were from C. Roth (Karlsruhe, Germany); naringenin, hesperetin, caffeine, salicin, and all other chemicals were from Sigma-Aldrich (Deisenhofen, Germany). Dried Herba Santa (*Eriodictyon californicum*) was from Alfred Galke GmbH (Gittelde, Germany). NMR spectra were recorded using Varian VXR400S (^{1}H: 400 MHz) spectrometer (Varian, Darmstadt, Germany) at 25 °C using tetramethylsilane as internal standard. LC-MS spectra were recorded using the LCQ HPLC system Finnigan MAT HP1100 (Finnigan MAT, Egelsbach, Germany; APCI atmospheric pressure chemical ionization). HT-GCMS (high-temperature GCMS) were performed on a 10 m DB-1HT short column (0.1 μm, i.d. 0.25 μm, Agilent, Böblingen, Germany) using cold injection and a temperature program starting at 80 °C increasing 12 °C/min to 380 °C on a Carlo Erba HRGC 5300; MS detection was done using a Finnigan MAT 8200 (Thermo Finnigan GmbH, Bremen, Germany). Chiral HPLC was performed on a Chiracel OD column (150 × 2.1 mm, Daicel Chiral Technologies Europe, Illkirch, France) using the eluent *n*-heptane/ethanol 87.5:12.5 (v/v, isocratic) at ambient temperature and detection with a DAD on a Merck-Hitachi D 6000 (Merck-Hitachi, Darmstadt, Germany). Water content was determined by Karl Fischer titration by the Analytical Department of Symrise, Symrise, Germany. Elemental analysis (combustional analysis for C, H, and O and AAS for sodium) was performed by Bayer Technology Services (Leverkusen, Germany).

Isolation of Homoeriodictyol Sodium Salt 1-Na from Herba Santa. Herba Santa (100 g, dried) was extracted with ethyl acetate (1300 mL) using a Soxhlet apparatus for 10 h. The solution was concentrated to 40% solid matter (dry weight) at <40 °C in vacuo and stored at 4 °C overnight. The leaf waxes were filtered off and analyzed separately. The resulting filtrate was treated with a ice cold sodium carbonate solution (450 mL, 10%). The resulting thick yellow precipitate was filtered off (3.95 g) and recrystallized from hot water to yield 1.96 g of homoeriodictyol sodium salt as pale yellow needles (HPLC 96%). A portion was recrystallized from acetone/water (3:1) for elemental analysis.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.05 (d, 1, J = 2.0 Hz, H-2′), 6.89 (dd, 1, J = 8.1 Hz, J = 2.0 Hz, H-6′), 6.80 (d, 1, J = 8.1 Hz, H-5′), 5.67 and 5.64 (AB-system, 2, H-6 and -8), 5.22 (dd, 1, J = 12.5 Hz, J = 3.0 Hz, H-2), 3.87 (s, 3, O−CH_3), 2.99 (dd, 1, J = 16.9 Hz, J = 12.5 Hz, H-3), 2.58 (dd, 1, J = 16.9 Hz, J = 3.0 Hz, H-3) ppm. ^{13}C NMR (100 MHz, CD_3OD, + DCl): δ = 196.38 (C, C-4), 166.74 (C, C-5, 7, or 9), 163.33 (C, C-5, 7, or 9), 162.87 (C, C-5, 7, or 9), 147.53 (C, C-4′), 146.90 (C, C-3′), 129.41 (C, C-1′), 119.64 (CH, C-6′), 115.19 (CH, C-5′), 111.14 (CH, C-2′), 101.70 (C, C-4a), 95.85 (CH, C-6 or 8), 95.07 (CH, C-8 or 6), 78.69 (CH, C-2), 55.71 (CH_3, O−CH_3), 42.11 (CH_2, C-3) ppm. MS (HPLC-MS, APCI+): m/z = 301.20 (100%), 302.15 (16.1%), 303.07 (3.9%). The water content (Karl Fischer) of 3.32% corresponds to 0.4−0.5 mol of H_2O/mol. Anal. Calcd for $C_{16}H_{13}O_6Na\cdot 0.5H_2O$: C, 57.67; H, 4.23; O, 31.20; Na, 6.90. Found: C, 57.85; H, 4.45; O, 31.25; Na, 6.45. $[\alpha]^{20}_D = \pm 0°$ (c = 10 g L^{-1}, acetone/H_2O, l = 1 dm).

Isolation of Sterubin 2. The organic phase of the filtrate (500 mL) from a homoeriodictyol precipitation (starting from 400 g of Herba Santa) was evaporated at <40 °C in vacuo to 50 mL and the precipitate filtered off. The crude sterubin was treated with hot ethyl acetate (80 mL), filtered again, and washed with diethyl ether to yield 3.2 g of pale yellow crystalline sterubin (HPLC 94%).

^{1}H NMR (400 MHz, CD_3OD): δ = 6.92 (m, 1, H-2′), 6.79 (ddd, 1, J = 8.2 Hz, J = 2.2 Hz, J = 0.4 Hz, H-6′), 6.78 (dd, 1, J = 8.2 Hz, J = 0.3 Hz, H-5′), 6.05 (d, 1, J = 2.3 Hz, H-6), 6.03 (d, 1, J = 2.3 Hz, H-8), 5.32 (dd, 1, J = 12.6 Hz, J = 3.1 Hz, H-2), 3.87 (s, 3, O−CH_3), 3.10 (dd, 1, J = 17.2 Hz, J = 12.6 Hz, H-3), 2.74 (dd, 1, J = 17.2 Hz, J = 3.1 Hz, H-3) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 198.27 (C, C-4), 169.59 (C, C-7), 165.29 (C, C-5), 164.74 (C, C-9), 146.99 (C, C-4′), 146.59 (C, C-3′), 131.68 (C, C-1′), 119.32 (CH, C-6′), 116.29 (CH, C-5′), 114.77 (CH, C-2′), 104.11 (C, C-4a), 95.74 (CH, C-8), 94.98 (CH, C-6), 80.71 (CH, C-2), 56.31 (CH_3, O−CH_3), 44.18 (CH_2, C-3) ppm. MS (HPLC-MS, 95:5 H_2O/acetonitrile, 5 min, 5:95 in 30 min, 15 min isocratic, ESI+): m/z = 303.190 (100%, $[M + H]^+$), 304.09 (17%), 305.17 (2%). $[\alpha]^{20}_D = \pm 0°$ (c = 10 g L^{-1}, acetone/H_2O, l = 1 dm).

Chiral HPLC Analysis of Flavanones. The test solutions were injected on to a Chiracel OD (150 × 2.1 mm) column and eluted with the isocratic solvent system 87.5:12.5 *n*-heptane/ethanol (v/v). Peak detection was performed by the UV-DAD. The flavanones eluted between 10 and 25 min. For direct analysis from plant material the herb was extracted with methanol at room temperature; the resulting solution was evaporated at ambient temperature in vacuo and dissolved prior to injection.

Sensory Studies. For screening of bitter masking the test compounds were added directly to an aqueous solution of the appropriate bitter compound; occasionally the mixture was treated for several minutes in an ultrasound bath to improve the dissolution process. Panelists (healthy adults, no tasting problems known) were trained on caffeine as bitter standard. Studies were performed in the morning hours 1−2 h after breakfeast during which time they were not allowed to drink black or green tea or coffee due to adaption to caffeine; only one bitter test/day was performed. For calibration the test persons used standard dilutions of caffeine (50, 100, 150, 200, 250, 300, 350, 400, 450, and 500 ppm). A minimum of 8 testers was used in the descriptive test. The bitterness was rated against the standard dilutions or on a scale of 1 (no bitterness) to 10 (very strong bitterness). Mean rating of a 500 ppm caffeine solution ranges between 6 and 7. For other bitter tastants concentrations were used at which all persons can perceive a pronounced bitterness (rating about 7). In the case of linoleic acid, a system containing 0.4 g of free fatty acid, 0.02 g of sucrosestearate, and test substance in 100 mL of water was emulsified using an Ultraturrax (Ika,

Table 1. Main Peaks of Isolated Leaf Waxes from *Eriodictyon Californicum* in HT-GCMS (10 m DB-1HT df, 0.1 μm; I.d., 0.25 μm; Cold Injection; Temperature Program 80–12–380 °C)

RI	intensity (%)	MS
2701	7.9	$C_{27}H_{56}$
2796	3.7	$C_{28}H_{58}$
2921	37.5	$C_{29}H_{60}$
2928	17.3	$C_{29}H_{60}$
2996	1.2	$C_{30}H_{62}$
3098	4.1	$C_{31}H_{64}$
rt 22.5 min	5.6	tetradecyloctadecanoate

Germany). For all experiments the test solutions were coded and in the case of color or cloudiness covered. Panelists were advised to test randomly mixed samples in the given order by the sip and spit method.

Statistics. The raw sensory data were analyzed using the standard functions of Microsoft Excel 97. For calculations of significance Student's matched pair tests were used.

RESULTS AND DISCUSSION

The isolation of homoeriodictyol was performed using a variation of the procedure originally described by Geissmann (*18*). Due to the handling of large quantities of diethyl ether, we decided to evaluate safer solvents. Ethyl acetate was a well-performing alternative for extraction of flavanones in high yields from the dried herb. After concentration of the solution the leaf waxes precipitated on cooling. The waxes consists mainly of paraffins, especially isomers of $C_{29}H_{60}$ as determined by high-temperature GCMS (HT GCMS, cf. **Table 1**). In the ^{1}H NMR spectrum only a singlet at 1.26 ppm and a triplet at 0.88 ppm (intensity approximately 10:1) were detectable. Thus, the alkanes are mainly of the straight chain type.

Following the dewaxing step, homoeriodictyol (**1**) was directly precipitated using sodium carbonate solution in 1.5−2.5% yield (related to the weight of dry plant material used). Starting from the filtrate, sterubin (**2**) was isolated by concentration and chilling (yield 1−2%).

The structure of isolated **2** was verified by NMR and HPLC MS experiments, and the data are consistent with the literature (*19*). The spectra of **1-Na** showed a highfield shift of roughly 0.4 ppm for the protons at positions 6 and 8 on ring A. After addition of a small amount DCl in methanol the shift values were identical with published data for **1** (*20*). Thus, we concluded that we have isolated a sodium salt of homoeriodictyol (**1**). The sodium content determined by elemental analysis was about 6.45%, which corresponds to the monosodium salt **1-Na**.

Krause and Galensa reported that the flavanones of plants exist mainly as (*S*)-enantionmers and are prone to racemization during workup (*21*). Indeed, the chiral analysis of commercial samples of naringenin and hesperitin as well as of isolated **1-Na** and even a crude methanolic extract from Herba Santa performed using a Chiracel OD column resulted only in a minor enantiomeric excess in the crude extract for **1** (cf. **Table 2**). In addition, no rotation of **1-Na** and **2** (Na-D) was detectable. These results also correspond to the findings of Yenesew et al., who found that 4′-hydroxyflavanones often racemize during isolation and workup (*22*).

The sodium salt **1-Na** and the flavanones homoeriodictyol **1**, sterubin **2**, hesperetin **3**, eriodictyol **4**, and naringenin (*4′*,5,7-trihydroxyflavanone) were evaluated as masking agents against caffeine in aqueous solution (cf. **Figure 2**), test concentration 500 ppm. At this concentration all testers perceive a strong bitterness. In contrast to the earlier findings (*15*), our own studies

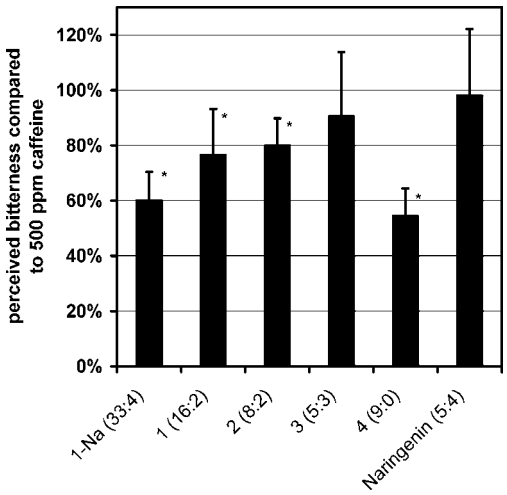

Figure 2. Perceived bitterness of solutions containing 500 ppm caffeine and different flavanoids (100 ppm) compared to pure caffeine. In parentheses are the numbers of test persons who rate the test solution lower and higher, respectively, compared to standard. Error bars represent 95% confidence intervals. Asterisks indicate significance $p < 0.05$.

Table 2. Chiral HPLC on Different Flavanone Preparations (Chiracel OD 150 × 2.1 mm; 87.5:12.5 (v/v) *n*-Heptane/Ethanol Isocratic)

sample	rt peak 1 (min)	intensity peak 1 (%)	rt peak 2 (min)	intensity peak 2 (%)
naringenin	12.7	49 (baseline)	14.2	49 (baseline)
hesperetin **3**	20.2	48	21.4	50
1-Na	18.1	51	19.2	49
crude methanolic Herba Santa extract	19.1	36	20.6	61

clearly show that the main flavanones from Herba Santa are able to decrease bitter taste. Eriodictyol **4** and **1-Na** showed the most remarkable masking effects against caffeine. The sodium salt of homoeriodictyol was chosen to conduct an in-depth testing. Formal methylation of **1** at position 7 yields sterubin **2** which showed only a weak activity against caffeine. When the vanillyl moiety of homoeriodictyol was changed to the isovanillyl pattern, as exemplified in hesperetin **3**, the activity decreased to some extent. The lack of a 3′-hydroxy or alkoxy group caused loss of activity as shown for naringenin.

In **Figure 3**, a dose−response of **1-Na** against caffeine bitterness is shown. Following a steep increase between 50 and 100 ppm, the activity reaches a plateau corresponding to a perceived bitterness comparable to 200 ppm caffeine. The masking effect obviously is only partial. Interestingly, we were not able to detect a masking agent which can fully block the perceived bitterness of caffeine or other bitter molecules.

In the course of the last 5 years the understanding of physiology of taste and especially of bitter taste perception and transduction in mammals has made great advances (*23*, *24*). Now it is clear that a set of about 24 different human bitter-sensitive G protein coupled receptors is expressed in taste cells, which are broadly tuned to several structural classes. For example, the human bitter receptor hTAS2R16 is able to bind selectively bitter tasting aromatic β-glucosides such as salicin (*25*, *26*). Thus, it is of interest to test potential bitter masking agents against different classes of bitter molecules. Therefore, we chose molecules which differ widely in structure and perhaps also in detection mechanisms (**Figure 4**): for quinine (*27*) and caffeine (*28*) mechanisms which are independent of the hTAS2R receptor family are still discussed in the literature, denatonium

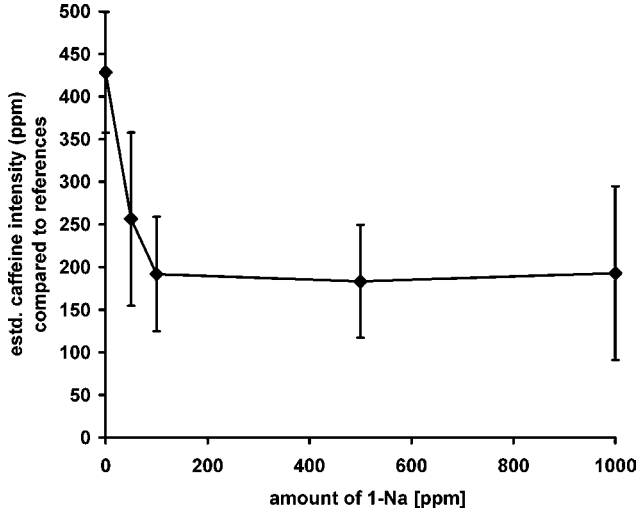

Figure 3. Dose–response curve of homoeriodictyol sodium salt **1-Na** in 500 ppm caffeine aqueous solution. The perceived bitterness is compared to reference solutions (100, 150, 200, 250, 300, 350, 400, 450, 500 ppm). Error bars represent 95% confidence intervals.

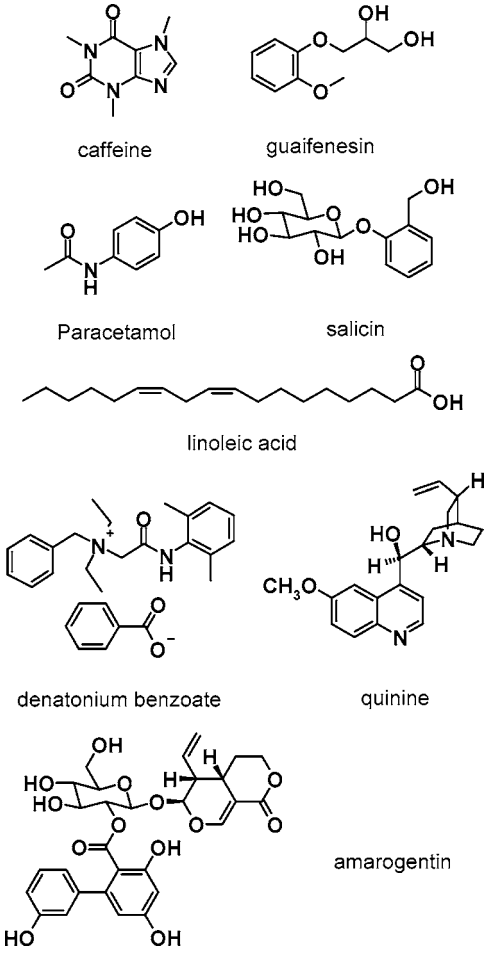

Figure 4. Structures of bitter compounds tested.

benzoate and amarogentin are described as extremely bitter (*29*), emulsions of free unsaturated fatty acids can cause bitterness in food (*30*), paracetamol and guaifenesin are widely used as over the counter drugs (*29*), and salicin belongs to the above-mentioned group of selective hTAS2R16 agonists (*26*).

All the mentioned bitter molecules were tested in different concentrations prior to masking experiments. In the following experiments, a concentration was chosen at which the rating of

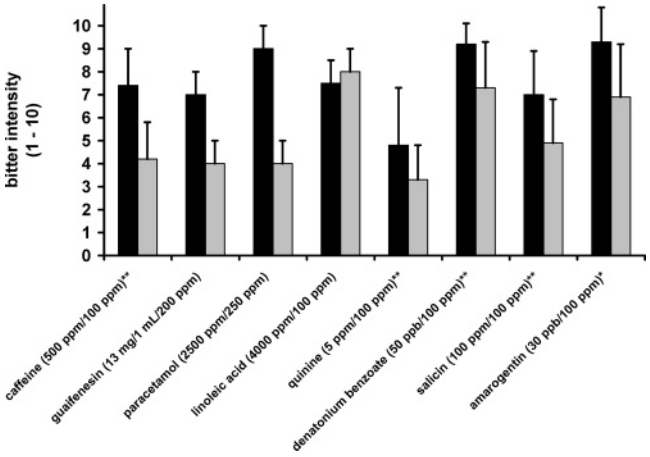

Figure 5. Masking ability of **1-Na** toward different bitter molecules. The perceived bitterness was rated on a hedonic scale of 1 (weak) to 10 (strong). Panelists randomly tested first pure bitter or first **1-Na**/bitter solution. The concentrations of bitter substance/**1-Na** are given in parentheses. Closed bars represent pure bitter solutions; error bars represent standard deviations. Significance: (*) $p < 0.05$; (**) $p < 0.005$.

bitterness was between 6 and 10 (1−10 scale) for more than 50% of the panelists. Linoleic acid when tested as a pure compound showed no bitterness. When the acid was administered in the form of an emulsion, a pronounced bitter taste was detected by the panelists. In most experiments some panelists (but not always the same!) showed an exceptionally low bitter rating (1−3 for pure bitter components), but their test data were not omitted. These "hypotasters" were able to perceive relative masking effects as well as "normal" panelists. In some cases we have performed the statistic calculations without using the data for "hypotasters", but the relative results for masking activity were not significantly influenced; only the calculated mean ratings increased to some extent.

The results of the masking experiments for homoerdiodictyol sodium salt (**1-Na**) against different bitter molecules are presented in **Figure 5**. In all cases with the exception of linoleic acid emulsion a reduction of the perceived bitterness was detectable. For the strongly bitter compound amarogentin, we performed a dose−activity study analogously to caffeine (cf. **Figure 6**). A slight increase of inhibitory activity was found, and the plateau was reached at 200−500 ppm **1-Na**. The maximum activities against caffeine and amarogentin bitterness were similiar (30−40% reduction).

All evaluated flavanones were tested for their taste and flavor profile at a concentration of 100 ppm in water and 5% sugar solution as exemplified in **Table 3**. Considering the relatively high concentration, the taste profiles showed no strong flavors or taste characteristics. Especially no strong bitter or astringent notes were detectable. Homoeriodictyol sodium salt (**1-Na**) showed no significant influence on sweet or salty taste characteristics, as determined in aqueous 5% sucrose (cf. **Table 3**) and 0.5% sodium chloride solutions (data not shown).

1-Na and probably the other active flavanones only partially block bitter reception. Therefore, it may be assumed that the blocker does not compete with bitter molecules on taste receptors but binds to a second (allosteric?) site common to all bitter receptors. Because it is known now that some bitter tastants can differently bind to more than one hTAS2R type (*31*, *32*), someone can suggest that the flavanones block one receptor type which shows an affinity to several bitter molecules. Alternatively, the flavanones may influence the signal transduction mechanism in the taste cell, but this is questionable

Table 3. Taste/Flavor Profile of Flavanones (100 ppm, 6–10 Panelists, Free Discussion)[a]

sample	flavor profile (1 weak to 9 strong)	
	aq soln	5% sugar soln
Homoeriodictyol sodium salt (**1-Na**)	vanillic (4), phenolic (3), balsamic (3), lactone (3), bitter (2), intensity (4), impact (3), mouthfeel (4), tenacity (4)	sweet (4), vanillin (4), flowery (2), phenolic (2), balsamic (3), intensity (5), impact (5), mouthfeel (4), tenacity (4)
homoeriodictyol (**1**)	sweet (3), vanillic (5), phenolic (5), herbal (5), balsamic (5), intensity (5), impact (4), mouthfeel (4), tenacity (5)	sweet (6), vanillin (3), phenolic (2), intensity (3), impact (3), mouthfeel (4), tenacity (4)
sterubin (**2**)	sage (5), woody (4), herbal (4), bitter (2), dry-dusty (4), intensity (5), impact (5), mouthfeel (3), tenacity (5)	bitter (3), dry-dusty (3), honey (4), herbs (3), intensity (4), impact (4), mouthfeel (4), tenacity (4)
hesperetin (**3**)	sweet (4), dry-dusty (3), balsamic (4), vanillic (3), intensity (4), impact (4), mouthfeel (3), tenacity (3)	soapy (4), sweet (6), bitter (2), chemically (4), intensity (5), impact (4), mouthfeel (3), tenacity (5), metallic (3), off-note (3)
eriodictyol (**4**)	coffee (4), bell pepper (5), herbal (3), intensity (4), impact (3), mouthfeel (4), tenacity (4)	sweet (4), intensity (3), impact (2), mouthfeel (3), tenacity (2)
naringenin	dry-dusty (4), fatty (4), creamy (3), intensity (4), impact (3), mouthfeel (4), tenacity (4)	sweet (4), rock candy (3), caramelic (3), broath (4), dry-dusty (3), intensity (3), impact (3), mouthfeel (5), tenacity (3)

[a] The sweetness of a 5% sucrose solution was rated 5 in average.

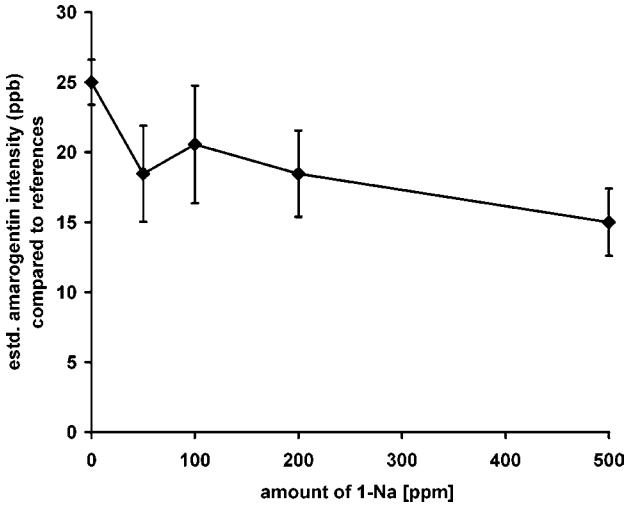

Figure 6. Dose–response curve of homoeriodictyol sodium salt **1-Na** in 30 ppb amarogentin aqueous solution. The perceived bitterness is compared to reference solutions (10, 15, 20,25, 30 ppb). Error bars represent 95% confidence intervals.

because of the lack of effects on sweet taste, which is probably transduced by the same second messenger system (phospholipase C-β/inositol phosphate) (*33*).

In conclusion, the flavanones homoeriodictyol (**1**), its sodium salt **1-Na**, and eriodictyol (**4**) isolated from Herba Santa show remarkable bitter masking effects without exhibiting any additional strong taste or flavor. Especially, **1-Na** seems to be a very interesting new taste modifier for food applications and pharmaceuticals. Further studies to clarify the mechanism of the inhibition will be performed.

ABBREVIATIONS USED

AAS, atomic absorption spectroscopy; AMP, adenosine monophosphate; hTAS2R, human taste receptor type 2; HT GCMS, high-temperature GCMS

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