

A Supplement Supporting Appetite Based on Olfactory Stimulation

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Abstract An olfactory supplements are used to influence the smell of foodstuffs in such a way as to make them olfactorily more attractive. The authors suggest the supplement for olfactory stimulation in patients with parenteral nutrition. The 25 panellists did not know what aromata were contained in the bottles, their concentrations, or the number of different samples presented to the panel. The aromata of the olfactory supplement were selected in such a way as to cover, due to its popularity, all spectrum of panellists: smoked ham, tangerine, Niva cheese and placebo. The parameters were evaluated either visually by an analogue scale from -10 to +10: pleasantness, smell, the sensation produced by the supplement, or the selection of the best corresponding verbal descriptor of the smell. The data were evaluated statistically. Comparison of the set was performed using the Mann-Whitney U test at the level of significance of alpha 0.05. All aromata under evaluation differed statistically significantly from placebo. Of the offered possibilities, however, only Tangerine was evaluated as pleasant: Z(4.5) for the supplement concentration of 1% and/or Z(5.2) for the 0.3% solution. The pleasantness of Niva cheese and smoked ham aromata were evaluated as not statistically different from placebo. No difference was found in olfactory preference in males and females.

Keywords: olfactory stimulation, sensory panel, nutrition, food, olfactory supplement

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1. Introduction

New pieces of knowledge indicate that nutrition through an oesophageal probe or percutaneous endoscopic gastrostomy (PEG) especially in geriatric and severely ill patients may result in the prevention of aspiration with subsequent respiratory infections. In patients with this type of nutrition there is a lack of stimulation of the olfactory epithelium by aroma and the oral mucous membrane by taste. [1] The stimulation of smell increases the quality of life of patients with head and neck cancer. [2] Moreover, if the olfactory or gustatory epithelium are stimulated, there occurs, besides increased activity of the upper swallowing tract [3,4,5], also an increase in blood flow through the digestive system, without necessary swallowing of food, which demonstrates that stimulation of the senses of smell or taste operates independently of stimulation of the abdomen or intestine by the swallowed food. [6] With regard to this, it can be expected that artificial support of the sense of smell and appetite improves intake of food, which is important especially in patients with feeding tube. [7]

Stimulating the sense of smell and appetite by means of food induces increased formation of saliva and other digestive agents. There are substantially more experiments dealing with the theme of the influence of the taste of foodstuffs on digestion than those dealing with the influence of aroma on the digestive process. [8] The present trial aims to propose such an olfactory supplement which could be used to stimulate the sense of smell in patients with food intake disorders, for example patients who are fed parenterally or by a feeding probe. In this group of patients when receiving food the olfactory sensation, which is the physiological stimulator of digestive functions, is eliminated. The introductory experiment focuses on the development of the form, composition and concentration of an olfactory supplement. After receiving the proper set of aromata, the experiments will continue in clinical nutritional studies. In future the use of a supplement is planned for patients with food intake disorders, primarily oncological patients with tumours of the head and neck during and after treatment.

2. Methods

Design: randomized double-blind clinical trial.

Ethics: We declare that the study have been approved by the Ethical Committee of University hospital Hradec Kralove and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

The substance tested: an olfactory supplement

The olfactory supplement which is being tested is a dietary supplement employed to influence the aroma of foodstuffs to make them "olfactorily more attractive". These supplements are routinely used substances employed to season the final products of food industry. Of the offered variants, the following aromata were selected:

1. Smoked ham
2. Tangerine
3. Niva cheese
4. Placebo (without aroma).

The below-mentioned amounts of the olfactory supplement were ordered and supplied by a firm for the trial. Two concentrations of each aroma were employed.

1. 10 times smoked ham 100 mg
2. 10 times smoked ham 300 mg
3. 10 times tangerine 100 mg
4. 10 times tangerine 300 mg
5. 10 times Niva cheese 100 mg
6. 10 times Niva cheese 300 mg
7. 10 times an empty bottle - placebo – thus just for water

Form of application: microemulsion in a 50 microlitre spray applicator. Each applicator is labelled with a random four-digit number.

Preparation: Olfactory stimulators were manufactured in the form of microgranules, on the surface of which an active substance was bound. They were supplied in a powdered form. Distilled water was used to dilute the olfactory supplements and served also as placebo. Not later than 2 hours prior to the beginning of the sensory panel, water was supplemented into prepared small bottles up to the gauge line of 100 ml, which achieved the required concentration. The solution prepared in this manner was not stabilized by any other chemical substance which would influence the olfactory sensation. It was not biologically stabilized either and had to be consumed on the same day. The used small bottles were destroyed after the trial.

Concentration of the olfactory supplement was selected in such a manner as to make the olfactory sensations very low and thus the minimal stimulatory concentration could not be exceeded. In order to verify the efficiency, the concentrations of 0.1% and 0.3% were selected. In each of the aromata 1-4, 2 concentrations were tested, i.e. altogether 8 aromata (including placebo). The panel always received 2 samples of each aroma and concentration, i.e. altogether 16 samples – with different random numbers. The amount of placebo 4 was employed because of the statistical equality of the sets. If wanting to evaluate, e.g., Tangerine (0.1 as well as 0.3 %) versus placebo, the number in the placebo branch would have to be sufficient.

3. Panel of Experts

Methodology of testing was used according to [9]

The tested supplement was presented to physicians employed at the Clinic of Otorhinolaryngology and Head

and Neck Surgery and the students of general medicine, who had been instructed in advance what they should evaluate in the tested sample. To avoid the bias, the panellists did not know what aromata were contained in the small bottles, what their concentrations were, or how many different samples were presented to the panel.

The panellists had to comply with the following criteria:

1. They must not suffer from a respiratory infection or a disease which impairs olfaction
2. They must not chew a chewing gum 30 minutes prior to testing
3. They must not eat spicy food prior to testing
4. On the day of testing they must not use perfume
5. On the day of testing they can use only an unperfumed deodorant
6. Prior to testing they must not use perfumed cosmetics, soaps, eau-de-Cologne, etc.
7. They must not have smelling compounds (disinfection) on their hands
8. They must not wear smelling clothes (medical personnel uniform is enough)
9. They must keep confidentiality of the panel
10. They must not influence other panellists by comments on the given sample

Each panellist was issued a random number and a form in which he/she evaluated the assigned samples. Each form included 8 items marked with random numbers. For each item the same parameters were evaluated.

3.1. Parameters under Evaluation

Pleasantness is subjective and is evaluated on a step scale by means of a visually analogue model (-10, 0, +10).

Unpleasant -10 -9 -8 -7 -6 -5 -4 -3 -2 -1 0 +1 +2 +3 +4 +5 +6 +7 +8 +9 +10 Pleasant.

3.2. Characteristics of Aroma

Panellists were to select a taste similar to the given supplement.

1. Salty (faintly 0+1+2+3+4+5 strongly)
2. Sweet (faintly 0+1+2+3+4+5 strongly)
3. Bitter (faintly 0+1+2+3+4+5 strongly)
4. Sour (faintly 0+1+2+3+4+5 strongly)
5. None (faintly 0+1+2+3+4+5 strongly)

3.3. Characteristics of the Sensation Induced by the Supplement:

1. Tingling (faintly 0+1+2+3+4+5 strongly)
2. Itching (faintly 0+1+2+3+4+5 strongly)
3. Warm (faintly 0+1+2+3+4+5 strongly)
4. Burning (faintly 0+1+2+3+4+5 strongly)
5. Pungent (faintly 0+1+2+3+4+5 strongly)
6. Sharp (faintly 0+1+2+3+4+5 strongly)
7. Cool (faintly 0+1+2+3+4+5 strongly)
8. Metallic (faintly 0+1+2+3+4+5 strongly)

3.4. Recognized Descriptors of Aroma

Panellists of each offered group of aromata selected at least one which according to their opinion was most similar to the presented supplement.

1. Floral

Almond, cinnamon, coconut, eucalyptus, fragrant, herbal, lavender, perfume, rose-like, spicy, vanilla

2. Fruity

Apple, cherry, citrus, cloves, grapes, lime, melon, maple, melon, minty, orange, strawberry

3. Medicinal

Alcohol, ammonia, anaesthetic, camphor, chlorinous, disinfectant, menthol, soapy, vinegar

4. Chemical

Car exhaust, cleaning liquids, creosote, gasoline, grease, kerosene, molasses, mothball, oil, paint, petroleum, plastic, solvent, sulphur, tar, turpentine, varnish, vinyl

5. Fishy

Ammine, dead fish, perm solution

6. Offensive

Blood, burn, decay, fecal, garbage, manure, putrid, rancid, raw meat, rotten eggs, septic, sewer, sour, urine, vomit

7. Earthy

Ashy, chalk like, grassy, mold, mouse like, mushrooms, musky, musty, peat like, pine, smokey, stale, swampy, woody, yeast

8. Vegetable

Celery, cucumber, dill, garlic, green pepper, nutty, onion

3.5. Statistical Evaluation

Statistical evaluation used the programme Statistica: version 13.2. All the mentioned parameters of tested samples were compared with placebo (saline solution). Distribution of the values in the set did not show normal distribution; that is why the non-parametric Mann-Whitney U test was used for the sake of comparison. Statistical significance was evaluated on the level of $\alpha=0.05$. The Z coefficient shows how many times the average monitored parameter was higher/lower than the identical parameter of placebo. The p value shows statistical significance. Statistically significant values of $p<0.05$ are in red.

4. Results

The results are depicted in tables 1.-6. A 0.1% solution containing tangerine aroma was compared with placebo. Even this very low concentration of aroma possesses a clearly dominating pleasant sour and stimulating tone, which dominates with the descriptors: floral and fruity. [Table 1.](#)

A 0.3%, solution containing tangerine aroma was also compared with placebo. A clearly dominating pleasant sweet, sour, fruity and stimulating tone. A number of panellists surprisingly classified the aroma as vegetables. [Table 2.](#)

A 0.1% solution containing smoked ham aroma was compared with placebo. In the evaluation of the supplement there dominate the items salty, irritating, pervasive, sharp, earthy and repulsive character. [Table 3.](#)

Higher concentration, a 0.3% solution containing smoked ham aroma was also compared with placebo. In the evaluation of the supplement there dominate the items

salty, stimulating, pervasive, sharp, earthy and repulsive character. The evaluation does not differ too much from the supplement with the low concentration of the aroma. [Table 4.](#)

Table 1. Mann-Whitney U test. A 0.1% solution containing tangerine aroma in comparison with placebo. Even this very low concentration of aroma possesses a clearly dominating pleasant sour and stimulating tone

Tangerine 0,1%. Mann-Whitney U Test,
Marked tests are significant at $p < 0,05000$

	Z	p-value
Pleasantness	-4,49176	0,000007
Salty	0,26194	0,793369
Sweet	-3,28878	0,001006
Bitter	-0,46567	0,641453
Sour	-3,26938	0,001078
None	2,26043	0,023795
Tingling	-1,27089	0,203770
Itching	-2,52237	0,011657
Warm	-0,74701	0,455058
Burning	0,00970	0,992260
Pungent	-3,30819	0,000939
Sharp	-0,97014	0,331976
Cool	-2,87162	0,004084
Metalic	-0,25224	0,800858
Floral	-2,53207	0,011340
Fruity	-4,76340	0,000002
Medicinal	-1,23208	0,217920
Chemical	-0,04851	0,961312
Fishy	-0,00970	0,992260
Offensive	-0,74701	0,455058
Earthy	-0,17463	0,861374
Vegetable	-0,74701	0,455058

Table 2. Mann-Whitney U test. A 0.3%, solution containing tangerine aroma in comparison with placebo. A clearly dominating pleasant sweet, sour, fruity and stimulating tone. A number of panellists surprisingly classified the aroma as vegetables

Tangerine 0,3%. Mann-Whitney U Test, Marked tests are significant at $p < 0,05000$		
	Z	p-value
Pleasantness	-5,23877	0,000000
Salty	0,50447	0,613929
Sweet	-3,71565	0,000203
Bitter	-0,46567	0,641453
Sour	-4,00669	0,000062
None	2,26043	0,023795
Tingling	-0,78582	0,431976
Itching	-1,04775	0,294753
Warm	-0,49477	0,620761
Burning	0,00970	0,992260
Pungent	-3,89027	0,000100
Sharp	-0,97014	0,331976
Cool	-2,54177	0,011030
Metalic	0,00000	1,000000
Floral	-2,04700	0,040659
Fruity	-4,97683	0,000001
Medicinal	-1,25000	0,211300
Chemical	0,23283	0,815890
Fishy	-0,25224	0,800858
Offensive	-0,26194	0,793369
Earthy	-0,23283	0,815890
Vegetable	-0,97014	0,331976

Table 3. Mann-Whitney U test. A 0.1% solution containing smoked ham aroma in comparison with placebo. In the evaluation of the supplement there dominate the items salty, irritating, pervasive, sharp, earthy and repulsive character

Smoked Ham 0,1%. Mann-Whitney U Test, Marked tests are significant at $p < .05000$		
	Z	p-value
Pleasantness	-0,59179	0,553994
Salty	-4,25893	0,000021
Sweet	-0,02910	0,976781
Bitter	-0,23283	0,815890
Sour	-0,50447	0,613929
None	1,97909	0,047807
Tingling	-0,76641	0,443431
Itching	-2,76491	0,005694
Warm	-1,24178	0,214318
Burning	-1,15447	0,248309
Pungent	-2,78431	0,005365
Sharp	-1,69775	0,089556
Cool	0,65000	0,515696
Metalic	-0,25224	0,800858
Floral	-0,70820	0,478819
Fruity	0,21343	0,830991
Medicinal	-0,49477	0,620761
Chemical	-1,04775	0,294753
Fishy	-0,77000	0,441300
Offensive	-2,45446	0,014110
Earthy	-2,38655	0,017008
Vegetable	-1,52312	0,127729

Table 4. Mann-Whitney U test. A 0.3% solution containing smoked ham aroma in comparison with placebo. In the evaluation of the supplement there dominate the items salty, stimulating, pervasive, sharp, earthy and repulsive character. The evaluation does not differ too much from the supplement with the low concentration of the aroma

Smoked ham 0,3%. Mann-Whitney U Test, Marked tests are significant at $p < .05000$		
	Z	p-value
Pleasantness	-0,84402	0,398657
Salty	-4,96713	0,000001
Sweet	-0,54328	0,586938
Bitter	-0,94104	0,346686
Sour	-0,72761	0,466855
None	2,53207	0,011340
Tingling	-0,50447	0,613929
Itching	-2,26043	0,023795
Warm	-1,74626	0,080767
Burning	-1,66865	0,095189
Pungent	-3,38580	0,000710
Sharp	-1,45521	0,145611
Cool	0,72761	0,466855
Metalic	-0,25224	0,800858
Floral	-1,19328	0,232762
Fruity	-0,02910	0,976781
Medicinal	-0,70820	0,478819
Chemical	-0,82462	0,409587
Fishy	-0,99925	0,317676
Offensive	-3,44401	0,000573
Earthy	-1,35820	0,174401
Vegetable	-2,00819	0,044623

A 0.1% solution containing Niva cheese aroma was compared with placebo. This very low aroma concentration also possesses a clearly dominating salty, pervasive, earthy, sharp, sweet and slightly repulsive character. [Table 5.](#)

A 0.3% solution containing Niva cheese aroma was compared with placebo. With the increased concentration of the aromatic substance in the supplement there occurred a marked difference between the tested substance and the placebo. Salty, pervasive, earthy and slightly repulsive character dominates.

Table 5. Mann-Whitney U test. A 0.1% solution containing Niva cheese aroma in comparison with placebo. This very low aroma concentration also possesses a clearly dominating salty, pervasive, earthy, sharp, sweet and slightly repulsive character

Niva cheese 0,1%. Mann-Whitney U Test, Marked tests are significant at $p < .05000$		
	Z	p-value
Pleasantness	-0,07761	0,938137
Salty	-1,95969	0,050033
Sweet	-2,65819	0,007857
Bitter	-0,93134	0,351680
Sour	-1,73656	0,082467
None	1,99849	0,045664
Tingling	-1,02835	0,303786
Itching	-1,81417	0,069653
Warm	-0,49477	0,620761
Burning	-0,22313	0,823432
Pungent	-3,34699	0,000817
Sharp	-0,97014	0,331976
Cool	-1,18357	0,236583
Metalic	0,00000	1,000000
Floral	-1,17387	0,240447
Fruity	-1,53283	0,125320
Medicinal	-0,70820	0,478819
Chemical	-0,27164	0,785899
Fishy	-0,25000	0,802588
Offensive	-1,95969	0,050033
Earthy	-1,73656	0,082467
Vegetable	-1,21268	0,225254

Table 6. Mann-Whitney U test. A 0.3% solution containing Niva cheese aroma in comparison with placebo. With the increased concentration of the aromatic substance in the supplement there occurred a marked difference between the tested substance and the supplement. Salty, pervasive, earthy and slightly repulsive character dominates

Nive cheese 0,3%. Mann-Whitney U Test, Marked tests are significant at $p < .05000$		
variable	Mann-Whitney U Test (Redukce placebo NK_KS.sta) By variable Ammount Marked tests are significant at $p < .05000$	
	Z	p-value
Pleasantness	1,80447	0,071159
Salty	-3,68654	0,000227
Sweet	-1,32910	0,183818
Bitter	-0,95074	0,341737
Sour	-0,99925	0,317676
None	1,99849	0,045664
Tingling	-0,97014	0,331976
Itching	-3,62833	0,000285
Warm	-0,99925	0,317676
Burning	-0,23283	0,815890
Pungent	-4,45295	0,000008
Sharp	-1,69775	0,089556
Cool	0,65000	0,515696
Metalic	-0,48507	0,627626
Floral	-0,69850	0,484863
Fruity	-0,27164	0,785899
Medicinal	-0,73731	0,460935
Chemical	-1,34850	0,177499
Fishy	-0,70820	0,478819
Offensive	-2,20222	0,027650
Earthy	-3,03655	0,002393
Vegetable	-0,74701	0,455058

5. Discussion

The trial revealed that in the preparation of the identical foodstuff there were different results in digestion when the foodstuff was salty or sweet, which certainly also resulted from a different chemical composition of salt and sugar. [10] The above-mentioned fact was the reason why different aromata were searched for, namely the salty Niva and sweet tangerine aromata, in order to be able to compare the influence of the so-called salty and sweet stimulation in future.

In the food industry, testing directly on consumers is widely used to find the best readily marketable foodstuffs. [11] The customers themselves thus essentially specify how the final product should taste. Nevertheless, in the case of patients with an organic swallowing disorder the olfactory sensations can be completely different from those of the healthy population. This can be considered a weak point of our testing, and that is why we opted for testing in the form of a sensory panel.

Testing by means of a sensory panel is used in various branches of food industry. For example, testing of instant and freshly ground coffee prepared from the same raw material revealed significant differences, predictably, in favour of freshly ground coffee [12] Also in the set of the olfactory supplements tested, a significant difference between the individual components was demonstrated.

There is a relatively interesting idea of influencing the aroma of dried vegetables. In a trial concerned with the preparation of vegetable food it was recommended to enrich the diet prepared from dried vegetable with the aroma extracted from fresh vegetable. [13] There are also great possibilities of influencing wine aroma. [14] Perhaps the influence on the olfactory sensation by the aroma of fresh vegetable or fruit could produce best results in our patients. Of the presented selection of supplements, tangerine aroma was the most successful.

One of the assumptions, i.e. that males will prefer salty and meat aroma and females the sweet one, has failed to be demonstrated, which, however, corresponds with some data from the literature. On testing various foods, no difference has been found in the gustatory preference of males and females. [15]

One of the mediators which induce the feeling of satiety and satisfaction from the received food in the central nervous system is dopamine. A comparison of the level of dopamine produced in the brain in rats has demonstrated that without olfactory and gustatory stimulation the dopamine level is not increased, and on the other hand, the level of dopamine is increased after stimulation [16]. In the case that aroma and taste are not stimulated during food intake, dopamine level in the brain is not increased. In PEG nutrition, the organism therefore lacks a number of factors which, in addition to nutritional value, is provided by food. Newly, a taste-supporting supplement was tested for persons with food intake disorders [17].

In accordance with the theme "Hunger is a Bad Oncologist" recently discussed by the Clinic of Oncology and Radiotherapy, the authors of the project assume that stimulation of the senses of taste and smell in patients nourished by PEG may result in an improvement of nourishment parameters, quality of life and a decrease in

the number of comorbidities resulting from insufficient nourishment or imperfect digestion. The project also dovetails into the concept "Development of the Treatment of Patient with Head and Neck Tumours" announced by the European ORL Society.

6. Conclusion

The trial has demonstrated the usability of an olfactory supplement in healthy volunteers. A statistically significant difference has been demonstrated between placebo and olfactory supplements. A sensory panel has selected tangerine aroma as the most pleasant one. Further testing will aim at the research of the support of appetite with the use of the same or a similar preparation.

Declarations

Conflict of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval: The manuscript has been approved by Ethical Committee of University Hospital in Hradec Kralove. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments.

Informed consent: Formal consent is not required for this type of study

Raw data are available in Author.

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