Quantitative assessment of gustatory function 
in a clinical context using “taste films kit”

Study Protocol

Study No. : OC16EIS0149

Department of Otorhinolaryngology-Head and Neck Surgery, Incheon St. Mary’s Hospital, College of medicine, The Catholic University of Korea
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1. **Title of clinical study and phase**

Quantitative assessment of gustatory function in a clinical context using “taste films kit” (Investigator-Initiative Study)

2. **Clinical study institution and address**

Incheon St. Mary’s Hospital, College of Medicine, the Catholic University of Korea
665 Bupyeong 6 dong, Bupyeong-gu, Incheon, Korea

3. **Names, position, and department of principal investigator and subinvestigator/coinvestigator**

Principal investigator: Dong Hyun Kim,
- Position: Associate Professor, Department: Incheon St. Mary’s Hospital, College of Medicine, the Catholic University of Korea

4. **Name and position of managing pharmacist**

Not applicable

5. **Name of sponsor and address**

Not applicable

6. **Purpose of the clinical study (primary and secondary purposes)**

We have developed a taste test kit using edible films that can be stored for a longer period of time than the conventional solution-based taste test. This new taste test is
more convenient and can be used without regard to location.

**The primary purpose** is to examine whether the taste-film test is useful as a test of taste function by verifying whether the taste identification threshold are similar to those for the conventional taste test when used in actual practice.

**The secondary purpose** is to determine whether the taste detection time and the total time are shorter than those of the conventional taste test.

### 7. Background of the clinical study

1) Absence of a standardized taste test

Diagnostic criteria have been established and diagnostic testing has been standardized for many diseases, but the diagnosis of taste disorders remains difficult and limited. Some clinics examine taste function using an electric signal, but the equipment is expensive and the medical approach limited. In addition, there is no standard for the threshold measured in such tests for diagnosing taste disorders. A new evaluation standard and appropriate quality control are needed for the diagnosis of taste disorders.

2) Increased need for taste testing

The number of patients with taste disorders has been increasing with increases in the number of elderly people and those with chronic diseases. Poor oral hygiene, dry mouth, and smoking can also cause taste disorders. Women are mainly responsible for cooking, and they often attend hospitals because of taste disorders. However, the percentage of people with taste disorders above a certain level does not differ according to gender.

The diagnosis and treatment of taste disorders have not received the attention of
doctors in the past. Many otolaryngologic procedures, such as middle ear surgery, tonsillectomy, salivary gland surgery, and laryngeal microsurgery, are likely to cause taste disorders. However, there is no adequate examination method or diagnostic equipment for use in the clinic or laboratory, which means that taste disorders may go unnoticed or undiagnosed. We are working to develop a new diagnostic test to enable the faster and more accurate identification of taste dysfunction compared with the conventional taste test.

8. Clinical study product (name of ingredient, product name of the drug)

- Taste-film kit

Registration of domestic patent (title: Composition for testing taste sense, and film and kit comprising the same (No. 10-11 83248 / Registration date November 08, 2011))

- Manufacture of taste-film kit

Distilled water is heated to 60–80 °C and Pullulan, a film former, is dissolved completely using a stirrer. The emulsifier (polysorbate 80) and the ingredients for each taste are added. The kit comprises five different concentrations of each
substance representing sweet (sucrose), salty (NaCl), sour (tartaric acid), and bitter (coffee) tastes. To form the film, these solutions are thinly coated on a flat sterilized pan at a constant thickness of 150–200 μm and dried in a drying oven at 50–60 °C for 2–3 h. The dried film is cut into regular pieces measuring $2 \times 1.5$ cm and packed into a taste-film kit.

<table>
<thead>
<tr>
<th>Component content of the taste film</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Bitter taste</th>
<th>74.09%</th>
<th>74.08%</th>
<th>74</th>
<th>73.6</th>
<th>70.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emul. Oil</td>
<td>0.9</td>
<td>0.001</td>
<td>0.9</td>
<td>0.002</td>
<td>0.9</td>
</tr>
<tr>
<td>Coffee</td>
<td>0.001</td>
<td>0.004%</td>
<td>0.002</td>
<td>0.01%</td>
<td>0.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Salty taste</th>
<th>74</th>
<th>73.74</th>
<th>72.7</th>
<th>71.3</th>
<th>67.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emul. Oil</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
<td>1.25</td>
<td>0.9</td>
</tr>
<tr>
<td>NaCl</td>
<td>0.1</td>
<td>0.38%</td>
<td>0.56</td>
<td>1.37%</td>
<td>1.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sweet taste</th>
<th>74.09%</th>
<th>74.02</th>
<th>73.5</th>
<th>72.89</th>
<th>71.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emul. Oil</td>
<td>0.9</td>
<td>0.02</td>
<td>0.9</td>
<td>0.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Sucrose</td>
<td>0.01</td>
<td>0.04%</td>
<td>0.08</td>
<td>0.31%</td>
<td>0.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sour taste</th>
<th>74.09%</th>
<th>74.02</th>
<th>73.5</th>
<th>72.89</th>
<th>71.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emul. Oil</td>
<td>0.9</td>
<td>0.02</td>
<td>0.9</td>
<td>0.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Tartaric acid</td>
<td>0.01</td>
<td>0.04%</td>
<td>0.08</td>
<td>0.31%</td>
<td>0.6</td>
</tr>
</tbody>
</table>

<Samples of taste-film kit>
9. Indication

None.

10. Inclusion and exclusion criteria for subjects, targeted number of subjects, and study rationale

- Inclusion criteria

The study will be conducted for patients aged 18 and 60 who visit the Department of Otolaryngology, Incheon St. Mary’s Hospital, College of Medicine, the Catholic University of Korea. The subjects must meet the following two criteria.

1. no problems in taste function, as judged by the subject

2. no abnormal lesions in the mouth and no abnormality in the movement of the tongue, as judged by the clinicians

The investigator who will manage this study will obtain approval from the Institutional Review Board (IRB) before starting the study. The investigator will immediately report any changes occurring during the study to the IRB. Those patients who satisfy the inclusion criteria and voluntarily consent to participate in this study will be the participants in this study.

- Exclusion criteria

The following will be the exclusion criteria:

1. history of smoking

2. diabetes

3. history of neurological disorders
4. history of middle-ear surgery

5. dental treatment within the previous 48 h

**-Targeted number of participants and rationale:**

The number of samples was calculated using a clinical equivalence test to verify that the results of the conventional solution taste test and the new edible film kit test were equivalent at the recognition and discrimination thresholds.

- Level of significance: $\alpha = 0.05$

- Test power at 80%, $\beta = 0.2$

- Mean difference between two groups, $\mu_c - \mu_t = 0$

- Clinical significance criterion, $\varepsilon = 0.5$. (A mean difference between the thresholds of $\leq 0.5$ is not considered to be a significant difference.)

- Standard deviation, $\delta$: Twenty-five patients were enrolled in a pilot study, and the standard deviations of the detection threshold and identification threshold for each taste were obtained.

- Dropout rate = 0.1

- Sample size ratio for both groups, $\lambda = 1$

$$n_c = \frac{(z_{\alpha/2} + z_\beta)^2 \sigma^2 \cdot (\lambda + 1)/\lambda}{(\varepsilon - |\mu_c - \mu_t|)^2}$$

Sweet taste detection threshold: Standard deviation 0.94: Minimum sample size considering a dropout number of 62

Sweet taste identification threshold: Standard deviation 0.66: Minimum sample size considering a dropout number of 32
Sour taste detection threshold: Standard deviation 0.56: Minimum sample size considering a dropout number of 22
Sour taste identification threshold: Standard deviation 0.66: Minimum sample size considering a dropout number of 32
Bitter taste detection threshold: Standard deviation 0.63: Minimum sample size considering a dropout number of 28
Bitter taste identification threshold: Standard deviation 0.63: Minimum sample size considering a dropout number of 28
Salty taste detection threshold: Standard deviation 0.20: Minimum sample size considering a dropout number of 3
Salty taste identification threshold: Standard deviation 0.57: Minimum sample size considering a dropout number of 23

At least 62 subjects should be included in each group.

11. Duration of the clinical study
- October 1, 2015 to December 31, 2015: Passed the IRB of our hospital
- January 1, 2016 to December 31, 2017: Data collection
- January 1, 2018 to June 30, 2018: Statistical analysis and manuscript preparation

12. Methods of the clinical study
(administration method, administration dose, administration duration, and combination therapy), control group selection, and treatment method in the control group
- **Study method**

  - Setting of the test group: The test group subjects will be recruited according to the above-mentioned inclusion and exclusion criteria
  
  - Method of recruitment of subjects: The research and informed consent will be explained to the patients who visit the hospital and to those who want to participate in the research.

- **Combination therapy:** Not applicable

- **Method for random assignment**

  To reduce bias according to test order, randomized methods including a computer-generated random number table will be used to assign subjects to the new taste-film test or conventional taste test.

13. **Observation items, clinical laboratory test items, and observation methods**

- **Taste function test**

  - Taste identification threshold: The lowest concentration at which a taste is recognized and determined as the correct taste
  
  - Preparation of five solutions (No. 1 to No. 5) of NaCl (salty), tartaric acid (sour), sucrose (sweet), and coffee (bitter)
<table>
<thead>
<tr>
<th></th>
<th>No.1</th>
<th>No.2</th>
<th>No.3</th>
<th>No.4</th>
<th>No.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucrose</td>
<td>0.3%</td>
<td>2.5%</td>
<td>10%</td>
<td>20%</td>
<td>40%</td>
</tr>
<tr>
<td>NaCl</td>
<td>0.3%</td>
<td>1.25%</td>
<td>5%</td>
<td>10%</td>
<td>20%</td>
</tr>
<tr>
<td>Tartaric acid</td>
<td>0.02%</td>
<td>0.2%</td>
<td>2%</td>
<td>4%</td>
<td>8%</td>
</tr>
<tr>
<td>Coffee</td>
<td>0.001%</td>
<td>0.02%</td>
<td>0.1%</td>
<td>0.5%</td>
<td>4%</td>
</tr>
</tbody>
</table>

**Taste solution method**

The taste solution test is applied to six specific regions on the left and right sides of the tongue. The sweet taste is tested at the tip of the tongue, the sour and salty tastes on the lateral sides of the tongue, and the bitter taste on the posterior one-third of the tongue. The examiner moistens the swab with the taste solution and stimulates the tongue of the subject gently. The subject then selects the flavor from the written index table. Salty, sour, and sweet tastes are examined in random order, and bitter taste is tested last. The solution test is performed using the same five concentrations as the film test and is conducted sequentially starting from the lowest concentration. After the test is completed for both the left and right sides of the tongue with one taste, the mouth is rinsed with water and then another taste is tested.

**Method for using the taste-film kit**

Using forceps, a taste film is placed on the middle portion of the tongue, and the subject senses the taste after the film is dissolved by saliva. The subject selects the perceived taste from a written index table. Salty, sour, and sweet tastes are examined in random order, and the bitter taste is tested last. The taste-film kit test is performed...
using the five concentrations sequentially from the lowest to highest concentration. After the test for one taste is completed for the middle portion of the tongue, the mouth is rinsed with water and then another taste is tested.

- **Recording method**

1. Starting from the lowest concentration for each taste, the concentration is increased in sequence (No. 1 → No. 5). The identification thresholds are recorded. For example: (4)

2. When a subject senses a taste that differs from the reagent taste (dysgeusia), the number of the concentration of taste and the taste indicated by the subject are recorded. For example: (sour; original sweet)

3. If the subject cannot sense the taste for concentration No. 5, it is recorded as “–”. When a taste is identified for concentrations No. 1–3, the result is recorded as “Good”. When a taste is identified for concentration No. 4 or No. 5, the result is recorded as hypogeusia. When a taste cannot be identified for concentration No. 5, the result is recorded as ageusia.

- **Patient information record**

The study number, and the hospital number, sex, age, taste identification threshold, and total test time will be recorded for each participant.
14. Discontinuation and termination criteria

- Patients may discontinue participation in the study whenever they wish without any disadvantage or loss of benefit.
- The investigator may withdraw a patient from the clinical study at any time without patient consent if he or she judges that discontinuation is the best choice for patient.
- A patient may be withdrawn if he or she violates the compliance criteria.
- The sponsor of this clinical study may discontinue the entire study.
- Any patients who develop any injury or disease as a result of their participation in this study will be provided with the appropriate medical treatment. Depending on the situation, this treatment may be free of charge.

15. Efficacy evaluation criteria, evaluation method, and interpretation method (statistical analysis method)

- Evaluation method

1. Comparison of the identification thresholds for each of the four tastes for each test
2. Comparison of the total test time between the two test methods
3. Comparison of the detection time for each taste within the test method

- Interpretation method

Statistical analysis will be conducted using SPSS, and group comparisons will be carried out using the Student’s t test. The level of significance will be set at 0.05.
16. Safety evaluation criteria, evaluation method, and reporting method including side effects

According to previous reports, side effects such as complications of the conventional taste function test should not occur.
17. Informed consent form or exemption statement if exempted

Consent form

1. Title: Quantitative assessment of gustatory function in a clinical context using “taste films kit”

2. Principal investigator: Dong Hyun Kim

   Our research staff recommend that you to participate in this clinical study because you are a healthy adult (18 years of age or more) and you think your taste function is good.

3. Things to know about the purpose of the clinical study

   - One of our research staff will explain the purpose of this clinical study.
   - Participation in this clinical study is voluntary.
   - The decision to participate should be made solely by you.
   - You may decide not to participate in this clinical study.
   - You may decide to participate in this clinical study now or later.
   - You will not be disadvantaged, whatever you decide.
   - Before deciding to participate, please ask any questions you may have.

4. Whom should I ask?

   If you have any questions, doubts, complaints, or concerns about injury from this study, please discuss them with our research staff.

   Phone number: (032)280-5151
This study has been reviewed and approved by the Catholic University of Korea Incheon St. Mary’s Hospital Institutional Review Board (IRB). You may consult the Catholic University of Korea Incheon St. Mary’s Hospital IRB through the Catholic Medical Center IRB:

- When you have any questions, concerns, or complaints that have not been answered by research staff.
- When you have difficulty making contact with research staff.
- When you would like to talk with someone other than research staff.
- When you have questions about the rights of a subject in the clinical study.
- When you attempt to receive information regarding this clinical study or provide your opinion on it.

Contact details are as follows.

- Catholic Medical Center (CMC) IRB: (02) 2258-7864
- Catholic University of Korea Incheon St. Mary’s Hospital IRB: (032) 280-5371

5. What is the purpose of this study?

The purpose of this study is to develop and validate a standardized diagnostic kit that can be used more conveniently than conventional tests for the accurate diagnosis of taste function. The results of this study will provide useful information for developing convenient methods to assess taste function and dysfunction.
6. How long is the total study period?

The expected duration for each subject is estimated to be about 30 min, which includes the total time for the taste test.

7. What is the procedure for this study?

You will be given a conventional solution taste test and a new edible taste-film test. The conventional taste test will be applied to six parts of your tongue and will involve the tastes of sweet, salty, bitter, and sour at various concentrations. After the end of the test for one taste, you rinse your mouth with water, and the test for the next taste is performed in the same order. After the taste is stimulated on your tongue, you will select the taste from a written index table. The taste-film test can is performed by placing the film on the middle of your tongue and allowing it to melt through the action of saliva. As in the conventional taste test, you will then select the taste from the written index table of taste. If you have any questions about this procedure, please call us at (032)-510-5602.

8. What should I observe while participating in the clinical study?

When you take a taste test, you should point your finger at the index table according to the tester's instructions.

9. What are some expected risks or discomforts if I participate in the clinical study?

- Physical risk (e.g. adverse drug effect): rare
- Mental risk (e.g. resistance to clinical study, fear, etc.): extremely rare
• Risk of personal information (e.g. risk of private information exposure): extremely rare

• Legal risk (e.g. possibility of being prosecuted in relation to previous criminal history): extremely rare

• Social risk (e.g. possibility of social discrimination): extremely rare

• Economic risk (e.g. burden of expenses because of participation in the clinical study, risk of insurance contract cancellation, risk of unemployment, etc.): extremely rare

10. Alternative options if you do not want to participate in the clinical study

If you do not want to participate in this study, you do not need to take the taste test.

11. Personal information protection

Your personal information, including study participation records and medical records, will be managed so that it is only provided to the person in charge of the review of such information. However, it is difficult to guarantee that your data will be kept completely confidential. Related agencies, such as the KFDA or the Ministry of Health and Welfare, may browse your data and make copies of them. The study results may be published in the future, but your name and other personal information will be kept strictly confidential.
12. Discontinuation of participation in the clinical study

You may discontinue your participation in the study whenever you want without any disadvantage or loss of benefit. If you want to stop participating in the study at any time, please contact the investigator. The investigator will then conduct the discontinuation process.

The investigator may drop you from the clinical study at any time without your consent if he or she judges that discontinuation is the best choice for you, or if you violate the participant compliance criteria (e.g. if you do not complete the questionnaire). In addition, the sponsor of this clinical study may discontinue the entire study.

If new information that affects your health and welfare or continuing participation in the study becomes available, we will inform you.

If you acquire any injury or disease as a result of participating in this study, you will receive appropriate medical treatment. Depending on the situation, this treatment may be free of charge. If you need more information, please contact the investigator.
Consent Form

Quantitative assessment of gustatory function in a clinical context using “taste films kit”

Your signature below indicates that you consent to participate in this study, and your protected health information will be exposed and used.

________________________________________
Name of subject

________________________________________
Signature of subject Date

Do not sign after this date.

________________________________________
Signature of person who obtains consent Date

________________________________________
Name of person who obtains consent

Date of preparation: ________________________
18. Regulations on subject compensation
In principle, there is no monetary reward for participation in this clinical study.

19. Subjects' treatment, treatment criteria, and safety protection measures after the clinical study
The principal investigator expects few or no side effects, sequelae, or complications from each taste test.

20. Actions for safety and protection of subjects
The principal investigator will ensure the safety and protection of all patient participants, and if serious adverse events occur, they will be reported to the IRB.
21. Case report form

● Information Record

1. Registration number:
2. Gender/age:
3. Study number:
4. Date of test:

● Taste solution test

1. Taste identification test

![Taste solution test diagram](image-url)
2. Total test time: _____ minutes _____ seconds

3. Taste detection time

   - Sweet taste _____ seconds
   - Salty taste _____ seconds
   - Sour taste _____ seconds
   - Bitter taste _____ seconds

● Taste-film kit test

1. Taste identification test

   - Sweet taste (    /    )    Salty taste (    /    )
   - Sour taste (    /    )     Bitter taste (    /    )

2. Total test time: _____ minutes _____ seconds

3. Taste detection time

   - Sweet taste _____ seconds
   - Salty taste _____ seconds
   - Sour taste _____ seconds
   - Bitter taste _____ seconds
22. Other necessities for safe and scientific conduct of the clinical study

Not applicable

23. Clinical literature that can be used as a source for the current study (references)


