

Development and Validation of a Chemotherapy-Induced Taste Alteration Scale

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Taste alterations are a common side effect seen in 30%–75% of all chemotherapy recipients (Bernhardson, Tishelman, & Rutqvist, 2009; Hovan et al., 2010; Kanda, Iida, & Ohta, 1998). Taste alterations result in various forms of distress for patients, including aversions to certain foods, reduction in meal intake, and weight loss (Boltong & Keast, 2012), as well as malnutrition in severe cases (Ravasco, 2005). In addition, loss of sense of taste can lead to a decrease in interest and enjoyment in social interactions because food plays a crucial role in societal activities (Epstein et al., 2002). Other studies have reported that taste alterations are significantly related to worsened quality of life (QOL) as measured with the Functional Assessment of Cancer Therapy–General and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (Wickham et al., 1999; Zubernig et al., 2010). Therefore, taste alterations do not merely interfere with the functioning of the senses, but greatly influence QOL in patients with cancer, and management of taste alterations during cancer chemotherapy is essential.

For definitions of terms, see Figure 1. Proper management of the symptoms of taste alteration requires assessment. Established objective methods for that purpose include electrogustometry (Krarup, 1958), the filter paper method (Berling, Knutsson, Rosenblad, & von Unge, 2011), and the whole-mouth gustatory test (Yamaguchi, Endo, Sakai, & Yoshimura, 2002), which are used in otolaryngology. Those methods involve evaluating taste threshold using electric stimulations, filter paper disc, or taste solutions. Although those objective indices are effective in evaluating hypogeusia and ageusia, they cannot assess the subjective symptoms that are commonly observed in patients with cancer undergoing chemotherapy, including phantogeusia and cacogeusia. In addition, those objective assessments require specialized knowledge and skills that can only be administered by otolaryngologists or laboratory technicians with special training.

Purpose/Objectives: To develop an instrument to assess the specific symptoms of chemotherapy-induced taste alterations.

Design: Cross-sectional study.

Setting: Two outpatient chemotherapy centers in Kanto, Japan.

Sample: Convenience sample of 214 adult patients with chemotherapy-induced taste alterations.

Methods: Items on the chemotherapy-induced taste alteration scale (CiTAS) were developed by a qualitative study of patients with taste alterations, and the content validity of each item was assessed by a panel of specialized oncology nurses. Data were analyzed for item consistency using Cronbach alpha and construct validity using factor analysis.

Main Research Variables: Taste alterations, symptoms of discomfort, and impact of taste alterations on daily life.

Findings: An 18-item scale was developed with four dimensions identified through factor analysis: decline in basic taste, discomfort, phantogeusia and parageusia, and general taste alterations. The scale demonstrated excellent reliability (Cronbach alpha = 0.9) and test-retest reliability ($r = 0.94$, $p < 0.001$, $n = 28$), as well as good validity, which was indicated by its strong correlation with a visual analog scale of the impact of taste alterations on daily life ($r = 0.62$, $p < 0.001$) and by negative correlations with Short Form–8 quality-of-life measures (physical component summary, $r = -0.33$; mental component summary, $r = -0.47$).

Conclusions: The CiTAS enabled valid, reliable measurement of specific symptoms of chemotherapy-induced taste alterations.

Implications for Nursing: The CiTAS has potential as a clinical tool and also could be used as a measure of chemotherapy-induced taste alterations in future studies.

Knowledge Translation: The CiTAS may help evaluate the effectiveness of interventions to reduce the symptoms of taste alterations, such as administering zinc and self-care strategies.

In that context, the authors sought to develop a subjective assessment scale for comprehensively evaluating the taste alterations experienced by patients with cancer undergoing chemotherapy, with the aim of ensuring ease of use. More specifically, the authors wanted the

- **Ageusia:** loss of taste functions of the tongue
- **Cacogeusia:** unpleasant taste that does not originate from food or beverage
- **Hypogeusia:** decreased ability to taste
- **Parageusia:** abnormal sense of taste
- **Phantogeusia:** continuous abnormal taste in the mouth, usually bitter or metallic

Figure 1. Definitions of Taste Abnormalities

scale to be able to evaluate umami, or richness of taste. Umami is of special interest in oncology populations because of the high protein content of umami-rich foods (Boltong & Keast, 2012), but few studies have assessed the influence of chemotherapy on umami (Sánchez-Lara et al., 2010), demonstrating a need to establish methods of evaluation.

The purpose of the current study was to develop a chemotherapy-induced taste alteration scale (CiTAS) for comprehensive assessment of taste alteration symptoms in chemotherapy recipients. The scale was designed to be short enough for screening symptoms and used as a means to explore coping strategies and their effectiveness in managing taste alterations.

Methods

Development of a Candidate Scale

The conceptual framework of chemotherapy-induced taste alterations and their associated outcomes is available from the authors by request. Chemotherapy has a physical impact that can negatively influence functioning of patients' digestive tract, vagus nerve, taste buds, salivary gland, and oral mucosa. Such dysfunctions lead to symptoms of taste alteration, which can affect patients' daily life by reducing enjoyment of eating, leading to social challenges and a loss of appetite. The severity of those effects is influenced by patients' coping skills, the extent of support they receive from others, associated food culture, and food habit.

The candidate version of the CiTAS (Kano & Kanda, 2011) comprised 34 items evaluated on a five-point Likert-type scale. Semistructured interviews were conducted to identify symptoms of taste alteration in eight chemotherapy recipients. An item pool then was created from 25 items associated with the identified symptoms. Categorization and abstraction of the retrieved items were performed using an inductive approach to qualitative analysis. Conceptualization of the symptoms resulted in the formation of three constructs of symptoms of taste alteration, namely change in the ability to taste, discomfort, and oral functional alterations (Kano & Kanda, 2011). Change in the ability to taste comprised the subconstructs of hypogeusia, phan-

togeusia and parageusia, and heterogeusia. Discomfort included olfactory aversion, nausea, and anorexia, and oral functional alterations included dryness of mouth, difficulty in swallowing, and stomatitis. Preexisting symptom names such as phantogeusia and parageusia were adopted for subconstructs for which diagnostic constructs had already been established.

Based on a review of the literature, nine items were added deductively to each subconstruct to cover other related symptoms. For example, in addition to the item "difficulty tasting saltiness" in the hypogeusia category, items on sweetness, sourness, bitterness, and umami were added to cover all the basic tastes. The expression of the items and the content validity of each subscale and item were examined by a panel of six specialized oncology nurses with more than a year of experience administering chemotherapy. The expression of some items was revised on the basis of that examination.

Participants

To meet the minimum requirement of 200 participants for validation studies (Murakami, 2006), the authors recruited 245 adult patients with cancer aged 20 years or older who were undergoing chemotherapy at outpatient chemotherapy centers at two cancer hospitals and who experienced taste alterations. The study was approved by the research ethics committee of Gunma Prefectural College of Health Sciences in Japan. Information on the purpose of the study, content of the survey, voluntary participation, and confidentiality of personal information were provided to potential participants orally and in writing. Those who agreed provided informed consent by signing a research participation form.

Survey Content and Procedure

Questionnaires were distributed to consenting participants when they presented at the hospitals for chemotherapy. The questionnaires comprised the CiTAS, items on age and gender, items from the Japanese version of the Short Form-8 (SF-8[®]) QOL measure (Fukuhara & Suzukamo, 2004), and items assessing the impact of taste alterations on daily life using a 100 mm visual analog scale (VAS). The SF-8 is a comprehensive measure used to assess QOL that includes physical and mental component summary scores and eight subscales: general health, physical functioning, role limitations because of physical health, body pain, vitality, social functioning, mental health, and role limitations because of emotional health. The reliability of the Japanese version of the SF-8 was assessed by an alternate-form method as acceptable (Spearman $r = 0.56-0.87$), and it also met the standard criteria for content, construct, and criterion validity (Fukuhara & Suzukamo, 2004). Participants responded to the questionnaire at home seven days after receiving chemotherapy and returned their responses by mail.

Information on diagnosis, antitumor drugs received, and the period of chemotherapy was obtained from medical records. The survey was administered from January 2008 through March 2010.

Data Analysis

SPSS®, version 19, was used for all data analyses. Means and standard deviations were computed for each item. Ceiling and floor effects were examined based on the highest (5) and lowest (1) values of the mean plus standard deviation and the mean minus standard deviation. Among items with a floor effect, those with a mean minus standard deviation higher than 0.8 were retained because a purpose of the CiTAS was to screen symptoms.

Pearson correlation coefficient was calculated to determine correlations between items. Among pairs of items that showed a correlation higher than 0.7, heterogeusia, hypogeusia, and phantogeusia were clinically distinctive, and thus one item from each pair was eliminated.

Factor analysis was performed by maximum likelihood extraction using a promax rotation for items after the item analyses, which were sensitive for Heywood case detection. The level for retaining an item was set at a factor loading higher than 0.4. For items that had a factor loading higher than 0.4 for several factors, only those with high clinical use were retained. Oblique rotation was retained because correlations were assumed to exist between categories on the scale. The Kaiser-Meyer-Olkin measure was used to evaluate model validity.

Criterion-related validity was examined by comparing participants' CiTAS scores with their SF-8 scores. Pearson *r* was calculated for the CiTAS total score and for SF-8 summary and subscale scores. To examine discriminant validity, impact VAS values were divided into groups by quartile, and CiTAS subscale scores (total scores divided by the number of items) were compared. Pearson *r* was obtained from the CiTAS total score, namely the sum of the four subscale scores, and impact VAS values. Subscale scores were further compared among participants' 10 primary treatment regimens.

Cronbach alpha was obtained for the total scale and for each subscale as an index of reliability. For test-retest reliability, 28 participants undergoing treatment at one- or two-week intervals were tested after two consecutive treatments. Pearson *r* was obtained for the two total CiTAS scores.

Results

Participants

Of the 245 participants who consented to participate, 219 responded. Data analysis was performed using the data provided by 214 participants, as 5 were excluded because of deficient responses. The valid response rate

was 87%. Sample characteristics are shown in Table 1. The mean age was 59 years (SD = 11.3), with the oldest being aged 83 years. The mean period of chemotherapy was 7.6 months (SD = 9.5), and the mean impact VAS score was 49.8 (SD = 25).

Item Analysis

Of the 34 items included on the candidate scale, 16 were deleted and 18 were retained for the survey. Reasons for exclusion were floor effect (*n* = 13), high item-to-item correlation (*n* = 1), and low factor loadings (*n* = 2). All items in the candidate scale construct of oral functional alterations (e.g., difficulty swallowing, dryness of the mouth, inner mouth pain, oral cavity discomfort) were excluded.

Examination of Validity

The 18 retained items were analyzed and classified into a four-factor structure (see Table 2). No Heywood cases or communality estimates exceeded 1 in the selected model. A favorable value of 0.88 was shown for the Kaiser-Meyer-Olkin societal living index of model validity.

Bitterness, sourness, saltiness, sweetness, and umami were placed under decline in basic taste. Umami also

Table 1. Sample Characteristics (N = 214)

Characteristic	n	%
Gender		
Male	85	40
Female	129	60
Cancer site		
Breast	62	29
Colorectal	49	23
Stomach	34	16
Lymphoma	16	8
Ovarian	14	7
Pancreas	10	5
Uterus	9	4
Liver, gallbladder, or bile duct	7	3
Prostate	7	3
Lung	2	1
Other	4	2
Chemotherapy regimen		
Paclitaxel	41	19
Folinic acid, fluorouracil, and oxaliplatin	26	12
Paclitaxel and carboplatin	19	9
Tegafur, gimeracil, oteracil potassium, and paclitaxel	19	9
Epirubicin, fluorouracil, and cyclophosphamide	18	8
Gemcitabine	17	8
Docetaxel	15	7
Rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone	15	7
Folinic acid, fluorouracil, and irinotecan	14	7
Folinic acid and fluorouracil	8	4
Other	22	10

was associated with a high factor loading of 0.49 for general taste alterations, indicating that it is unique from the other basic tastes. Symptoms related to loss of appetite, such as difficulty eating meat or oily foods, aversion to smells, and nausea, were classified as discomfort. Parageusia, cacogeusia, and failure to distinguish flavors were classified as general taste alterations.

The CiTAS total score and the SF-8 physical component summary score had a correlation coefficient of -0.33 . The correlation of CiTAS total score and the SF-8 mental component summary yielded a coefficient of -0.47 , indicating a mild-to-moderate negative correlation, suggesting QOL tends to decline as taste alterations become stronger. Moderately significant relationships were seen for the SF-8 subscales, including role limitations because of emotional health ($r = -0.47$), mental health ($r = -0.45$), social functioning ($r = -0.44$), general health ($r = -0.43$), vitality ($r = -0.42$), and role limitations because of physical health ($r = -0.33$). In contrast, the CiTAS subscale of discomfort was rather strongly correlated with vitality ($r = -0.58$), social functioning ($r = -0.57$), mental component summary ($r = -0.56$), mental health ($r = -0.5$), general health ($r = -0.5$), role limitations because of emotional health ($r = -0.49$), and role limitations because of physical health ($r = -0.43$).

No strong correlation was observed between the CiTAS total score and the SF-8 overall score. However, examination of the subscales revealed a unique outcome, namely that changes in taste negatively influence QOL, thus demonstrating the usefulness of the CiTAS and supporting its criterion-related validity.

The impact VAS score was divided into groups by quartile to examine the discriminant validity of CiTAS, and subscale scores then were compared (see Figure 2). All subscale scores were elevated for groups reporting a strong impact of taste alterations in daily life. A strong correlation was observed between the CiTAS total score and the impact VAS score ($r = 0.62$, $p < 0.001$).

A comparison of the subscale scores for each therapy regimen revealed high scores for general taste alterations and phantogeusia and parageusia for R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone) therapy, which is used to treat lymphoma (see Figure 3). High discomfort and phantogeusia and parageusia scores were associated with paclitaxel plus carboplatin, which is used to treat ovarian cancer, and FEC (epirubicin, fluorouracil, and cyclophosphamide), which is used to treat breast cancer. The results matched the patients' clinical reports. A comparison of FEC and docetaxel, also used in the

treatment of breast cancer, revealed that although discomfort was markedly low for docetaxel, general taste alterations increased. That finding is consistent with reports from patients with breast cancer who are switched from FEC to docetaxel, and with a study comparing gustatory function after chemotherapy with FEC and FEC plus docetaxel (Steinbach et al., 2009).

Cronbach alpha was 0.9 (overall) for the 18 items, and a positive outcome of 0.8–0.86 was shown for the four subscales. A comparison of the total scores from a second test of 28 participants performed to examine test-retest reliability yielded $r = 0.94$ ($p < 0.001$).

Discussion

The aim of the current study was to develop a clinically applicable self-report survey instrument that would be useful for comprehensive evaluation of taste alterations in patients with cancer undergoing chemotherapy. Symptoms related to chemotherapy-induced taste alterations reported

Table 2. Factor Matrix Following Promax Rotation for Items on the Chemotherapy-Induced Taste Alteration Scale (N = 214)

Variable	α	Factor			
		1	2	3	4
Factor 1: Decline in basic taste	0.85				
Have difficulty tasting bitterness		0.72	0.03	0.1	-0.04
Have difficulty tasting sourness		0.69	-0.08	0.13	0.09
Have difficulty tasting saltiness		0.64	0.02	0.04	0.05
Have difficulty tasting sweetness		0.63	0.06	0.09	0.01
Have difficulty tasting umami		0.53	-0.01	-0.16	0.49
Factor 2: Discomfort	0.8				
Have difficulty eating meat		0.11	0.84	-0.1	-0.09
Have difficulty eating oily food		0.17	0.82	-0.05	-0.15
Have a reduced appetite		-0.05	0.54	-0.01	0.27
Have difficulty eating hot food		0.06	0.51	0.01	0.03
Bothered by the smell of food		-0.22	0.49	0.1	0.18
Feel nauseated or queasy		-0.17	0.45	0.17	0.05
Factor 3: Phantogeusia and parageusia	0.85				
Have a bitter taste in the mouth		0.2	-0.01	0.96	-0.24
Everything tastes bitter		0.05	-0.04	0.71	0.18
Have a bad taste in the mouth		-0.02	0.08	0.62	0.18
Factor 4: General taste alterations	0.86				
Food doesn't taste as it should		0.08	-0.01	-0.04	0.84
Everything tastes bad		-0.14	0.1	0.34	0.66
Have difficulty tasting food		0.37	-0.1	-0.07	0.64
Unable to perceive the smell or flavor of food		0.13	0.09	-0.02	0.56

Note. The level for retaining an item was set at a factor loading higher than 0.4 (maximum-likelihood extraction with promax rotation), indicated in bold.

in the literature include decreased ability to taste and metallic taste (Boltong, Keast, & Aranda, 2012; Ravasco, 2005), nausea and appetite loss (Bernhardson et al., 2009), food aversion and increased sensitivity to bitter taste (Ravasco, 2005), and difficulties related to sense of smell (Bernhardson et al., 2009). The CiTAS was designed to incorporate all the aforementioned symptoms, and as such, it may be used to assess taste alterations accompanying chemotherapy.

Selection of Scale Items

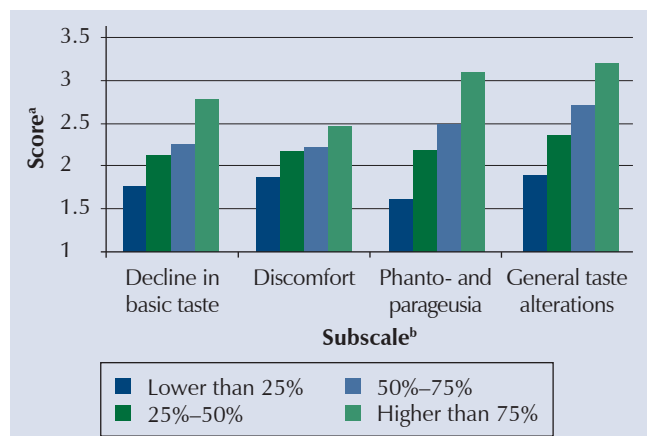
The wording of the CiTAS items was based on the three constructs of change in the ability to taste, discomfort, and oral functional alterations, which were derived from qualitative research with patients with cancer undergoing chemotherapy. The content was based on diagnostic constructs of impairments in taste and oral function, and covers symptoms specific to chemotherapy such as bitter taste and decreased appetite (Rehwaldt et al., 2009). As item validity and ease of comprehension were examined by specialized oncology nurses, the items adopted for CiTAS were considered easy to respond to, encompassing the characteristics of taste alterations accompanying chemotherapy, and conforming to preexisting diagnostic constructs.

In the item analysis, questions on oral function alterations were eliminated because of the floor effect. Floor effects for 10 items resulting from the use of various expressions suggested that taste alterations associated with chemotherapy have little effect on oral function alterations. Therefore, oral function alterations should not be adopted for the CiTAS but should instead be evaluated individually for patients experiencing those symptoms.

Reliability and Validity of the Scale

The proportion of patients with lung cancer in the sample was lower than for other cancers. The study focused on chemotherapy recipients who lived at home, and the number of patients with lung cancer receiving outpatient care is low in Japan (Yamada et al., 2011). In a qualitative study by Horiguchi et al. (2009), patients with lung cancer receiving platinum-based drugs reported morning sickness–like difficulties with smells, taste alterations for previously preferred foods, nausea, and vomiting. Those findings suggest that patients with lung cancer experience symptoms similar to those of patients with other types of cancer who are undergoing chemotherapy, supporting the results of the current study. Therefore, the small number of participants with lung cancer would not have affected the validity of the current findings.

The CiTAS demonstrated good internal consistency and good reproducibility. Items categorized under discomfort for the candidate scale were supported in



^a Lower scores indicate milder symptoms.

^b A higher percentile indicates a stronger impact of taste alterations on daily life.

CiTAS—chemotherapy-induced taste alteration scale; VAS—visual analog scale

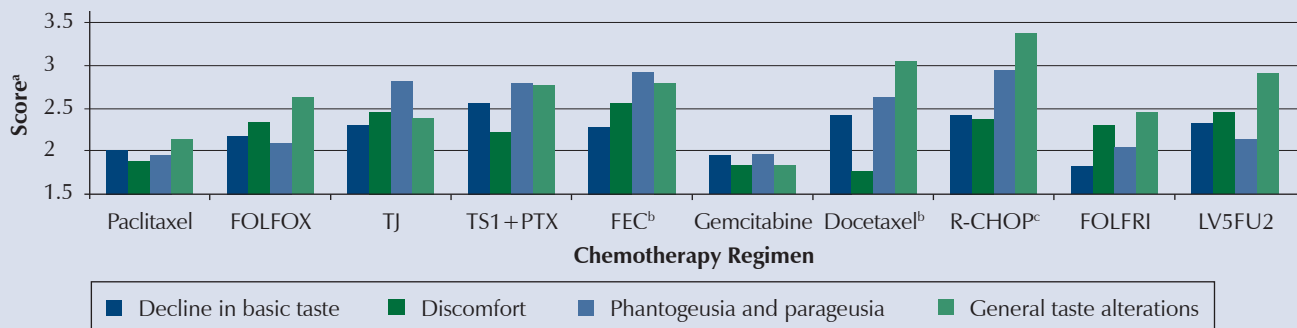
Note. All subscale scores were found to be elevated for groups reporting a strong impact of taste alterations. A strong correlation was observed between CiTAS score and impact VAS score ($r = 0.62$, $p < 0.001$).

Figure 2. Comparison of CiTAS Subscale Scores With Quartile Impact VAS Scores (N = 214)

the factor analysis. Items under change in the ability to taste were further categorized under decline in basic taste, phantogeusia and parageusia, and general taste alterations. Those three factors were consistent with the diagnostic constructs of taste disorders, thereby supporting the validity of the CiTAS. Although difficulty in tasting umami had a factor loading as high as 0.4 for general taste alterations, the item was considered clinically useful and, therefore, was retained. The strong relationship between difficulty in tasting umami and other factors suggests that the mechanism of that taste alteration may differ from those of other basic tastes, indicating its importance.

In the examination of criterion-related validity, mild-to-moderate negative correlations were observed between the CiTAS and SF-8. The greater the severity of symptoms of taste alterations, particularly those related to discomfort, the greater the decline in QOL. Those findings support the validity of the CiTAS.

In the examination of discriminant validity, comparisons of the impact VAS score for the groups divided by quartile showed that, when taste alterations had a strong impact on daily life, CiTAS mean subscale scores were higher. In addition, a strong correlation was observed between the CiTAS total score and impact VAS score. Comparisons of the subscale scores by treatment regimen were consistent with patients' subjective symptoms by treatment regimen, thus supporting the discriminant validity of the CiTAS.



^a Lower scores indicate milder symptoms.

^b A comparison of FEC and docetaxel, which are used for treating breast cancer, revealed discomfort was markedly low for docetaxel and general taste alterations were increased.

^c R-CHOP, which is used to treat lymphoma, was associated with the highest score for general taste alterations and phantogeusia and parageusia.

CiTAS—chemotherapy-induced taste alteration scale; FEC—epirubicin, fluorouracil, and cyclophosphamide; FOLFOX—folinic acid, fluorouracil, and oxaliplatin; FOLFRI—folinic acid, fluorouracil, and irinotecan; LV5FU2—folinic acid and fluorouracil; R-CHOP—rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone; TJ—paclitaxel and carboplatin; TS1 + PTX—tegafur, gimeracil, oteracil potassium, and paclitaxel

Figure 3. Relationship Between CiTAS Subscale Scores and Chemotherapy Regimen (N = 214)

Conclusions and Implications for Nursing Research

The CiTAS is the only self-report scale that comprehensively evaluates taste alterations induced by chemotherapy. The instrument is clinically applicable with high reliability and validity and has a favorable response rate. In addition, the scale takes only a few minutes to complete and patients reported it was easy to take. The CiTAS can be used in future nursing research and practice as an assessment tool for taste alterations in patients with cancer who undergo chemotherapy. The quality and extent of taste alteration can be evaluated without the need for specialized equipment or staff trained in measurement. In addition, the CiTAS may assist in evaluating the effectiveness of interventions directed at taste alterations, such as administering zinc (Yamagata et al., 2003) and self-

care strategies (Rehwaldt et al., 2009). The current study also revealed the type and extent of symptoms experienced with each chemotherapy regimen. The authors hope the CiTAS will bring about innovations for guiding patients toward self-management of chemotherapy-induced taste alterations.

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