













| Name | Photos | Pecen-tage (%) | Component | Experiments | Expected effects |
|-----------------------------|---|----------------|------------------------------|---|---|
| Citrus unshiu peel |  | 12 | Hesperidin | <ul style="list-style-type: none"> • Activation of CREB/ BDNF pathway in the hippocampus (59,66–73) | <ul style="list-style-type: none"> • Influence on sensory reweighting |
| Pinellia tuber |  | 12 | Alkaloids | <ul style="list-style-type: none"> • Influence on gastroesophageal vagal nodose C-fibers (58–60) | <ul style="list-style-type: none"> • Relieve nausea/vomiting and gastrointestinal discomfort |
| Atractylodes rhizome |  | 12 | Atractylenolide III | <ul style="list-style-type: none"> • Influence on gastroesophageal vagal nodose C-fibers (58–60) • Anti-diuretic effects (14,18,61,62) • Anti-depression effects (59,65) • Activation of CREB/ BDNF pathway in the hippocampus (59,66–73) | <ul style="list-style-type: none"> • Relieve nausea/vomiting and gastrointestinal discomfort • Improve hydrops in inner ear • Improve mood disorders • Influence on sensory reweighting |
| Atractylodes lancea rhizome |  | 12 | | | |
| Poria sclerotium |  | 12 | Triterpenes, Polysaccharides | <ul style="list-style-type: none"> • Anti-diuretic effects (14,18,61,62) | <ul style="list-style-type: none"> • Improve hydrops in inner ear |
| Gastrodia tuber |  | 8 | Vanillin | <ul style="list-style-type: none"> • Anti-depression effects (59,65) • Protection of hippocampal CA1 neurons against ischemic cell death, production of an increase in neuronal survival and antioxidant activity against lipid peroxidation (64) | <ul style="list-style-type: none"> • Improve mood disorders • Influence on sensory reweighting |
| Malt |  | 8 | Amylase | <ul style="list-style-type: none"> • Catalysation the hydrolysis of starch | <ul style="list-style-type: none"> • Improve gastrointestinal discomfort |
| Astragalus root |  | 6 | Astragaloside IV | <ul style="list-style-type: none"> • Anti-diuretic effects (14,18,61,62) | <ul style="list-style-type: none"> • Improve hydrops in inner ear |
| Alisma tuber |  | 6 | Triterpenoids | <ul style="list-style-type: none"> • Anti-diuretic effects (14,18,61,62) | <ul style="list-style-type: none"> • Improve hydrops in inner ear |
| Ginseng |  | 6 | Ginsenosides | <ul style="list-style-type: none"> • Anti-depression effects (59,65) • Activation of CREB/ BDNF pathway in the hippocampus (59,66–73) | <ul style="list-style-type: none"> • Improve hydrops in inner ear • Influence on sensory reweighting |
| Phellodendron bark |  | 4 | Berberine | <ul style="list-style-type: none"> • Cyclooxygenase-2 in anti-inflammatory activity (63) | <ul style="list-style-type: none"> • Improve hydrops in inner ear |
| Ginger |  | 2 | 6-shogaol | <ul style="list-style-type: none"> • Influence on gastroesophageal vagal nodose C-fibers (58–60) | <ul style="list-style-type: none"> • Relieve nausea/vomiting and gastrointestinal discomfort |

Supplementary Figure 1 Components and effects of hangebyakujutsutemmato. Hangebyakujutsutemmato is composed of 12 crude herbal extracts, each of which affects the human body. HBT, Hangebyakujutsutemmato.

Supplementary Table 1 Overview of the assessment tools used in this study and their respective scoring systems

| | Aim | Test | Scoring and criteria |
|----------------|-----------------------------|--|--|
| Questionnaires | Degree of vertigo/dizziness | DHI ^[24] | 100-point scale, 25 items |
| | Anxiety and depression | HADS ^[26] | Sub-grouped into three domains: Physical (P), Emotional (E), Functional (F) Anxiety (A) 21-point scale, Seven questions; Depression (D) 21-point scale, Seven questions |
| | OD | OD questionnaire ^[28,29] | 11-point scale, 11 questions |
| | Motion sickness | Graybiel's motion sickness scores ^[30] | 56-point scale, six questions |
| | Sleep quality | PSQI ^[31,32] | 21-point scale, 18 questions |
| Tests | Static postural stability | Foam Stabilometry The values of six parameters; the velocity of movement of the center of pressure (COP) (VCF) and envelopment area tracing by the movement of the COP in the eyes closed/foam rubber condition to assess vestibular weighting, Romberg's ratios of velocity and area with foam rubber (velocity; VRF, area; ARF) | VCF ACF VRF ARF VFCF AFCF Large VCF and ACF, and small VRF, ARF, VFCF, and AFCF indicated poor static balance |

to assess visual weighting, and the foam ratios (ratios of a measured parameter with to without the foam rubber) of velocity and area in the eyes closed condition (velocity; VFCF and area; AFCF) to assess somatosensory weighting^[41].

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| Dynamic postural stability (Foulage test; stepping test) | Foulage test ^[34-36,42] Stepping test: regulated 120 bpm tempo, upright standing with both arms set at the sides of the body, feet closed, toes touching the plate continuously so that the individual can change only the height of their heels to rise up alternatively. | FT value (area of the front-back width of the locus) with eyes open and closed ^[34,35,42] . |
| Otolith function (Saccule) | cVEMP ^[37] AR was defined as the difference between the large amplitude (AL) and small amplitude (AS) of peak 13 to peak n23 divided by the sum of both amplitudes presented as a percentage, | Small AR indicated good saccule-inferior vestibular nerve function |

i.e., $[(AL-AS)/(AL + AS)] \times 100$ (%). The normal range of AR was defined as less than 33%.

| | | | | |
|---|--|---|----------------------|--------------|
| Otolith function (Utricle) | <p>oVEMP^[44] AR was defined as the difference between the large amplitude (AL) and small amplitude (AS) of peak p11 to peak n15 divided by the sum of both amplitudes presented as a percentage, i.e., $[(AL-AS)/(AL + AS)] \times 100$ (%). The normal range of AR was defined as less than 33%.</p> | Small AR utricule-superior function | indicated vestibular | good nerve |
| Semicircular canal and otolith function (Utricle) | <p>Caloric test^[46] Canal paresis % (CP%) was calculated using the following equation: $[(MVS \text{ of the right warm (RW)} + MVS \text{ of the right warm (RW)}) - (MVS \text{ of the left warm (LW)} + MVS \text{ of the left cold (LC)})] / (RW + RC + LW + LC) \times 100$(%). The normal range of the CP% was defined as less than 20%.</p> | Small CP% (<20%) utricule-superior function | indicated vestibular | normal nerve |

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|----|---|--|
| OD | <p>HUT test^[40,80]</p> <p>The HUT test was performed according to the method established by the Japan Society of Neurovegetative Research in 2015^[29]. Non-invasive oscillatory measurements of blood pressure (BP) and the pulse rate were performed four times using an automated sphygmomanometer (ES-H55P; Terumo, Tokyo, Japan) at the following timepoints: (1) After 10 min in the supine position; (2) After 1 min of standing; and (3) After 10 min of standing^[29]. The cuff of the BP-recording device was attached to the left arm, which was supported at heart level throughout the study. Testing was conducted during the daytime in a quiet environment at a constant room temperature of</p> | <p>Results of the test were considered positive when meeting either of the following criteria: (1) BP drop $\geq 20/10$ mmHg 1 min, or 10 min after standing; HR ≥ 120/min or an increase of 30 beats/min over that in the supine position 1 min or 10 min after standing; and (2) For systolic BP, diastolic BP, heart rate, CVRR, HF, and LF/HF, the change ratios were calculated as a measured parameter of (2)/(1) for the immediate change ratio, and (3)/(2) for the delayed change ratio.</p> |
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22–25 °C to exclude the effects of chronobiologic factors on the outcomes of the test. The participants maintained a regular meal schedule but were restricted from smoking and caffeine ingestion for 6 hours before the examination. The intake of foods and medications with sympathomimetic activity was also prohibited before the study. The results were determined as positive or negative according to the outcome of the HUT test and the international scientific definition of OD

VOR Nystagmus: Nystagmus Positive if any nystagmus was observed
was evaluated using an
infrared CCD camera.
When pathologic
nystagmus (*i.e.*,
spontaneous nystagmus or
positional nystagmus) was
observed, the test result was
considered positive

DHI: Dizziness handicap inventory; HADS: Hospital Anxiety and Depression Scale; OD: Orthostatic dysregulation; PSQI: Pittsburgh Sleep Quality Index; FT value: Foulage test value; AR: Asymmetry ratio; cVEMP: Cervical vestibular-evoked myogenic potential; oVEMP: ocular VEMP; CP%: Canal paresis %; MVS: Maximum slow-phase velocity speed; HUT: Head-up tilt; VOR: Vestibulo-ocular reflex; HR: Heart rate; BP: Blood pressure.