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Comprehensive study on the impact of tea (*Camellia sinensis*) on human mental health

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Abstract:

Tea, particularly the green, black, and oolong varieties derived from the *Camellia sinensis* plant, is widely consumed across the globe and has been associated with neuroprotective effects in human studies. This research synthesised findings from 318 studies sourced from PubMed, with an emphasis on 18 relevant studies, to evaluate the impact of tea, including its constituents L-theanine and epigallocatechin gallate (EGCG), on brain function and neurodegenerative conditions such as memory loss and cognitive decline. The results from both intervention and observational studies indicate that tea positively influences psychological well-being, cognitive abilities, and brain function, particularly in reducing anxiety, enhancing memory, and improving attention. The analysis, conducted using the restricted maximum likelihood model, confirmed a beneficial effect size of 0.50 for tea, with no evidence of publication bias, underscoring its significance in promoting nervous system activity.

Keywords: **epigallocatechin gallate and cognitive function, L-theanine, neurodegeneration, tea consumption.**

Classification numbers: **3.2, 3.3, 3.5**

1. Introduction

Tea, derived from the plant species scientifically known as *Camellia sinensis* (L.) O. Kuntze, is one of the most widely consumed beverages globally. Green tea, black tea, and oolong tea originate from the same plant but undergo different processing methods, which vary depending on the degree of fermentation [1, 2]. The effects of tea have been extensively studied, revealing a wide range of benefits, including anti-cancer, anti-obesity, anti-diabetic, and anti-inflammatory properties, as well as protection against neurodegeneration [3].

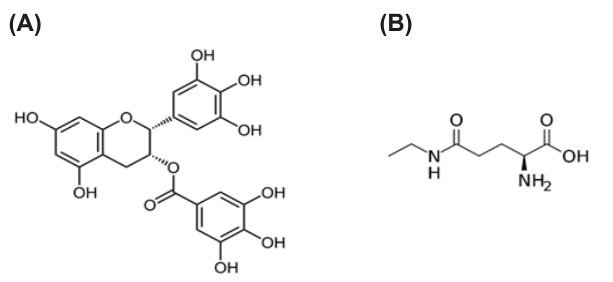

Fig. 1. Chemical structure of epigallocatechin gallate (EGCG) (A) and L-theanine (B) extracted from tea leaves (*Camellia sinensis*).

The chemical composition of tea is highly complex, with catechin compounds playing a particularly significant role in impacting human health and brain function. Among these catechins, EGCG is the most abundant, constituting 65%, followed by L-theanine, which makes up 4-6% (Fig. 1). These compounds, along with tea extracts, are known for their roles in cancer prevention, obesity control, diabetes management, anti-inflammatory effects, and protection against neurodegeneration [4]. Nervous system activity is a crucial area of research, particularly in relation to diseases and ageing. S.Q. Chen, et al. (2018) [5] have demonstrated the protective and supportive effects of tea components, including catechins, on nervous system function, suggesting their potential role in future treatments for neurodegenerative conditions.

In this study, we employed a meta-analysis approach to synthesise the findings of individual studies that varied in their assessments of the positive effects of tea and its two essential components, EGCG and L-theanine, on human nervous system activity. The research methodology was based on effect size estimation and the standard error, which represents the variance within the study samples in individual studies.

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2. Materials and methods

2.1. Constructing and establishing research data

Numerous databases, such as ScienceDirect, Springer Open, Wiley Open, Elsevier Open, NUiLibrary (United Nations iLibrary), Open Access, PLoS (Public Library of Science), MDPI (Publisher of Open Access Journals), and NLM (National Library of Medicine), are available for research purposes. Given our focus on specialised meta-analysis in healthcare and human health, NIH and PubMed were selected for this study. Data were obtained using relevant preliminary keywords and target population criteria; five criteria were established for the search results: (1) search results indicating positive impacts, (2) search results from fundamental or experimental studies, (3) search results from studies conducted on humans, (4) search results from *in vivo* studies, and (5) search results from studies influenced by tea extract and EGCG/L-theanine (Fig. 2).

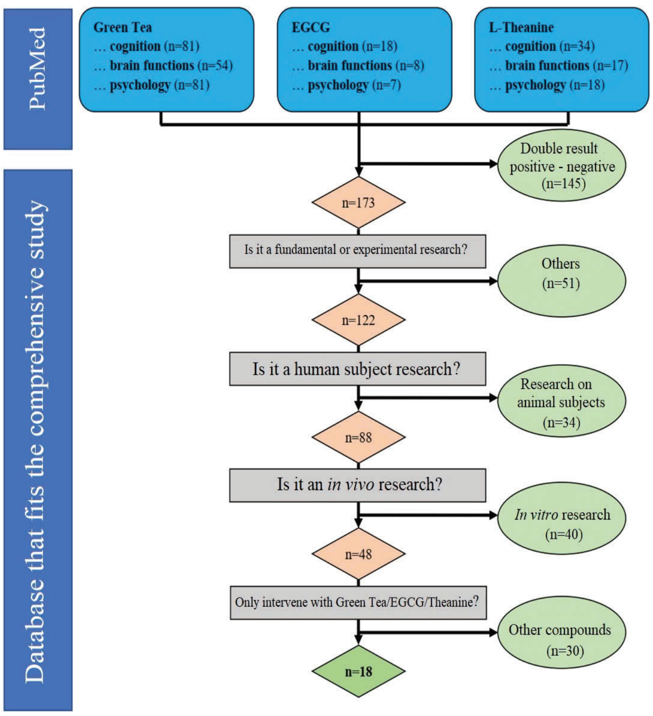

Fig. 2. Construction of database using PubMed data.

The retrieved documents were filtered using keywords. In cases where consistency was lacking, manual reviews by research team members were performed to ensure the accuracy and optimal quality of the data. Selected publications were required to meet all criteria precisely, avoiding keyword or selection biases. The criteria for selecting data sources were optimised for meta-analysis.

2.2. Targeted parameters

Given that studies often employed different models, some provided direct outcomes of interest, while others required indirect results to be calculated from other statistics such as t-tests, F-tests, correlation coefficients, p-values, or chi-squared values. Consequently, the final indices were often heterogeneous. Data transformation was, therefore, necessary before conducting an assessment model. Our meta-analysis focused on the study's effect size and standard error. Effect size is a unitless estimate indicating the direction and magnitude of the effect/result. The standard error measures the dispersion of different sample means taken from the same population and can be estimated from the standard deviation of a single sample within each study.

2.3. Analysis method and software used

The meta-analysis was conducted using JASP (Jeffrey's Amazing Statistics Program), a statistical software developed to acknowledge the contributions of Sir Harold Jeffreys, a pioneer in Bayesian statistics. JASP is a free, open-source, cross-platform statistical package developed and regularly updated by researchers at the University of Amsterdam (Netherlands). The software is widely used in meta-analysis due to its accessibility, versatility in simulating diverse studies, and practical assessment of research biases.

Effect sizes and standard errors were transformed from various outcomes in the collected studies using the "Practical Meta-Analysis Effect Size Calculator" developed by Dr. David Wilson. This software is a foundational resource for teaching in university statistics programmes. It is based on open-source platforms, such as that at George Mason University (America).

3. Results and discussion

3.1. Data collection

The data for this study were collected from the PubMed database, initially comprising 318 studies. Participating researchers refined this dataset through keyword selection and manual review. Ultimately, 18 studies were selected that met the specified criteria, including 14 intervention studies and four observational studies (Table 1).

Table 1. Suitable studies extracted from the PubMed database.

Study	No. of volunteers	Intervention therapy	Types of study
A) Volunteer healthy at the beginning of the study			
A. Schmidt, et al. (2014) [6]	12 (12 males, average age 24.1)	Green tea extract	Double-blind, controlled, intervention study
A. Scholey, et al. (2012) [7]	31 (12 males, average age 27.7)	Green tea extract + EGCG	Double-blind, controlled, crossover intervention study
E.L. Wightman, et al. (2012) [8]	27 (11 males, average age 22)	EGCG	Double-blind, controlled, crossover intervention study
M. Ota, et al. (2014) [9]	14 (7 males, average age 31)	L-Theanine	Double-blind, controlled, intervention study
A. Yoto, et al. (2012) [10]	16 (8 males, average age 22.8)	L-Theanine	Randomised, controlled, crossover intervention study
T. Giesbrecht, et al. (2010) [11]	44 (16 males, average age 21.2)	L-Theanine + Caffeine	Randomised, double-blind, controlled, intervention study
S.J. Einöther, et al. (2010) [12]	29 (11 males, average age 30.6)	L-Theanine + Caffeine	Randomised, double-blind, controlled, crossover intervention study
G.N. Owen, et al. (2008) [13]	27 (14 males, average age 28.3)	L-Theanine + Caffeine	Randomised, double-blind, controlled, intervention study
S.P. Kelly, et al. (2008) [14]	16 (11 males, average age 27.5)	L-Theanine	Intervention study with repetitive and intervention control
C.F. Haskell, et al. (2008) [15]	21 (9 males, average age 21.3)	L-Theanine	Double-blind, controlled, crossover intervention study
K. Kimura, et al. (2007) [16]	12 (12 males, average age 21.5)	L-Theanine	Double-blind, controlled, crossover intervention study
B) Volunteers with underlying medical conditions requiring immediate intervention			
S.K. Park, et al. (2011) [17]	91 (25 males, age groups 40-75 and 21-26)	Green tea extract + L-Theanine	Double-blind, controlled, intervention study
M.S. Ritsner, et al. (2011) [18]	60 (48 males, average age 36.5)	L-Theanine	Double-blind, controlled, crossover intervention study
A.L. Brown, et al. (2009) [19]	100 (100 males, age 40-65)	EGCG	Randomised, double-blind, intervention study
C) Healthy volunteers or volunteers with medical history but no requirement for immediate intervention, observation study of lifestyle and habits			
Y. Tomata, et al. (2012) [20]	23.091 (age >65)	Green tea extract	Observational study (3 years)
L. Feng, et al. (2010) [21]	716 (age >55, average age 64.5)	Green tea extract	Observational study
A. Hozawa, et al. (2009) [22]	42.093 (age >40)	Green tea extract	Observational study (3 years)
S. Kuriyama, et al. (2006) [23]	1003 (age >70)	Green tea extract	Observational study (4 years)

The 18 selected studies involved a total of 67,403 voluntary participants. Among these, 500 participants were included in the intervention studies, and 66,903 were part of the observational studies conducted over time. The 500 participants in the intervention studies were further classified into two categories based on their health conditions at the outset of the study: 249 individuals were in good health, while 251 individuals had underlying medical conditions requiring intervention.

3.2. Estimation of effect size and standard error

Effect size is a dimensionless measure representing the magnitude of the desired effect on the health of study participants, attributable to tea, EGCG, or L-theanine. Effect size was calculated using software based on the results from the 18 different studies. Standard error was used to estimate the dispersion of data within each study's sample. In this study, standard error represented the variability in the effects and influences of observational factors on the study participants (Table 2) [24].

Table 2. Effect size and standard error of the chosen studies.

No.	Author(s)	Year published	Effect size	Standard error
1	A. Schmidt, et al. (2014) [6]	2014	0.8960	0.4283
2	A. Scholey, et al. (2012) [7]	2012	0.7724	0.3724
3	E.L. Wightman, et al. (2012) [8]	2015	1.0988	0.4129
4	M. Ota, et al. (2014) [9]	2014	0.9258	0.5624
5	A. Yoto, et al. (2012) [10]	2012	0.9029	0.5249
6	T. Giesbrecht, et al. (2010) [11]	2010	0.9677	0.3186
7	S.J. Einöther, et al. (2010) [12]	2010	0.7259	0.3834
8	G.N. Owen, et al. (2008) [13]	2008	0.7775	0.3991
9	S.P. Kelly, et al. (2008) [14]	2008	1.3693	0.5555
10	C.F. Haskell, et al. (2008) [15]	2008	0.9670	0.4314
11	K. Kimura, et al. (2007) [16]	2007	1.0770	0.6178
12	S.K. Park, et al. (2011) [17]	2011	1.0547	0.4794
13	M.S. Ritsner, et al. (2011) [18]	2009	0.0047	0.3162
14	A.L. Brown, et al. (2009) [19]	2009	0.4588	0.2162
15	Y. Tomata, et al. (2012) [20]	2012	0.0088	0.0141
16	L. Feng, et al. (2010) [21]	2010	0.3371	0.0775
17	A. Hozawa, et al. (2009) [22]	2009	0.0169	0.0200
18	S. Kuriyama, et al. (2006) [23]	2006	0.0342	0.0742

The analysis revealed significant statistical dispersion among the studies, which can be attributed to the diversity in study types, sample sizes, and study durations. The variability in effect size and standard error not only reflected the heterogeneity of the studies but also depended on the results of the analysis of heterogeneity, adjusted effect size, and publication bias in the conducted meta-analysis.

3.3. Estimation of heterogeneity among studies

Heterogeneity in this study was assessed to construct an appropriate meta-analysis model. It was estimated by comparing fixed effect and random effect models using statistical hypothesis testing [25].

The null hypothesis (H_0) posited that all studies had the same effect (fixed effect), while the alternative hypothesis (H_1) suggested heterogeneity (random effect). The results indicated that the statistical hypothesis test was significant (p<0.01) (Table 3), leading us to proceed with further analysis. The random effect model was found to be statistically significant (p<0.001) (Table 4), providing grounds to reject H_0. Therefore, the effects of the studies in this meta-analysis varied under the alternative hypothesis H_1 (random effect).

Table 3. Statistical test of the hypotheses (Fixed and random effects).

	Q	df	p
Omnibus test of model coefficients	20.911	1	<0.001
Test of residual heterogeneity	75.973	17	<0.001

*: *p*-values are approximate, the model was estimated using a restricted machine learning method.

Table 4. Statistical test of the models (Coefficients).

	Estimate	Standard error	z	p
intercept	0.495	0.107	4.632	<0.001

*: Wald test.

Table 5. Statistical estimation of heterogeneity.

	Estimation
τ^2	0.120
τ	0.347
I^2 (%)	96.608
H^2	29.480

The analysis suggested that the fixed effect model was unsuitable for this study. Consequently, the restricted maximum likelihood model was chosen. This model estimates the parameter distribution of data by maximising the likelihood function, assuming that the synthesised data becomes most appropriate under the assumption of a positive effect of the material on the study participants [26]. Clinical and methodological diversity is inherent in meta-analyses, making statistical heterogeneity inevitable. The I^2 statistic was used in this study to assess heterogeneity, with the following interpretation: 0 to 40% might not be significant; 30 to 60% might represent moderate heterogeneity; 50 to 90% might indicate substantial heterogeneity; and 75 to 100% could indicate considerable heterogeneity [27].

To reinforce the hypothesis that the random effect model was optimal, the I^2 statistic was quantified. The random effect model was deemed suitable when the I^2 statistic was between 30 and 100%. The results indicated that I^2=96.608 (Table 5), confirming that the random effect model was appropriate for our study.

3.4. Meta-analysis validation

A forest plot was used to assess the results of the meta-analysis of the 18 studies. This plot aimed to confirm the initial hypothesis that the positive effects of tea and its extract compounds on the human nervous system are indeed significant, as quantified by effect size with a standard error for a 95% confidence interval. The random effect model chosen for this analysis was the restricted maximum likelihood model, which is advantageous for assuming an efficient treatment distribution across various sample groups with differing but related intervention effects. This model offers better balance when considering the weights of different studies, aiming to determine the average effectiveness of tea's impact on the nervous system. In the forest plot (Fig. 3), the horizontal line represents the length of the confidence interval, where a longer line indicates a wider confidence interval, making the study results less reliable. The vertical line represents the null effect line, also known as the line of no effect, indicating no clear difference between the intervention and control groups [28].

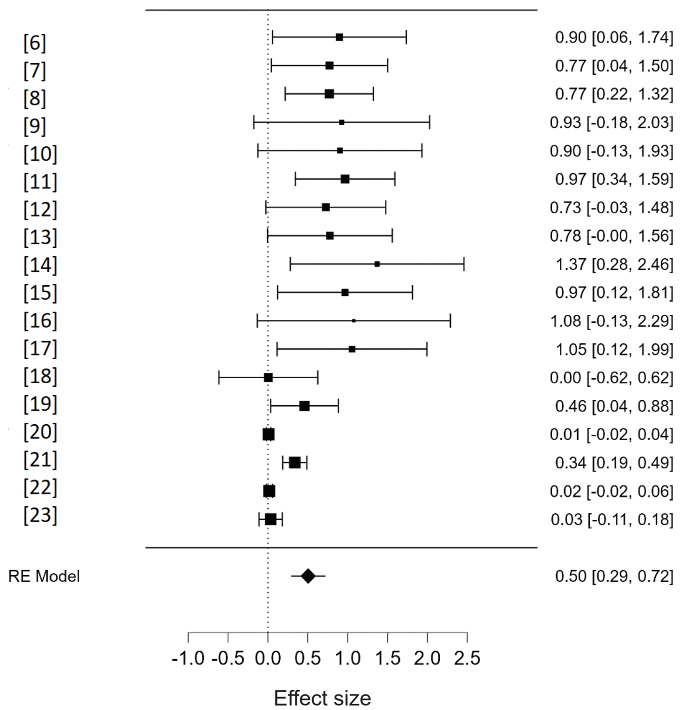

Fig. 3. Forest plot representing meta-analysis results.

Table 6. Estimation of outliers and statistical weight factors.

No	Std. residual	DFFITS	Cook's distance	Cov. ratio	$\tau^2_{(-i)}$	$Q_{E(-i)}$	Hat	Weight
14	0.728	0.157	0.025	1.035	0.119	71.861	0.040	4.006
15	0.532	0.100	0.010	1.064	0.123	71.971	0.047	4.698
17	0.605	0.139	0.019	1.077	0.123	69.043	0.061	6.086
10	0.647	0.112	0.013	1.027	0.120	73.422	0.028	2.787
18	0.643	0.116	0.013	1.031	0.120	73.192	0.031	3.074
4	1.048	0.319	0.098	1.006	0.112	67.258	0.055	5.484
2	0.429	0.066	0.004	1.071	0.124	72.654	0.046	4.552
11	0.522	0.094	0.009	1.059	0.123	72.441	0.044	4.352
7	1.371	0.312	0.095	0.966	0.110	70.138	0.028	2.838
5	0.862	0.201	0.040	1.021	0.117	71.230	0.040	3.971
8	0.823	0.147	0.022	1.011	0.118	73.088	0.024	2.424
12	0.960	0.218	0.047	1.007	0.116	71.382	0.035	3.475
13	-1.091	-0.312	0.101	1.098	0.127	75.968	0.055	5.522
1	-0.139	-0.135	0.020	1.165	0.135	71.987	0.073	7.281
16	-1.542	-0.458	0.195	1.060	0.112	71.087	0.101	10.089
3	-0.500	-0.269	0.083	1.209	0.138	59.701	0.096	9.625
6	-1.509	-0.456	0.195	1.067	0.113	75.545	0.101	10.072
9	-1.405	-0.439	0.188	1.089	0.117	75.965	0.097	9.664

The adjusted overall effect size for the studies was 0.50, with a 95% confidence interval of [0.29-0.72]. This result suggests that tea's impact on the human nervous system in the analysed studies was relatively substantial, with an estimated value of 0.50 (0.29-0.72). Among the studies, A. Schmidt, et al. (2010) [6] reported the highest effect size of 0.90 (0.06-1.74), while S. Kuriyama, et al. (2006) [23] reported the lowest effect size of 0.03 (-0.11-0.18). M.S. Ritsner, et al. (2010) [18] showed no significant contribution to the meta-analysis, as their effect size coincided with the null effect line, indicating no significant contribution to the combined analysis.

The intervention studies, both on individuals with health conditions and healthy individuals (studies 1-14 in Table 2), exhibited a wide range of variability and a large positive effect. In contrast, the observational studies without intervention over a long period with large sample sizes (studies 14-18 in Table 2) demonstrated lower variability and a smaller positive effect. Intervention studies are suitable for assessing the short-term effectiveness of clinical treatment processes on specific study samples, while large-scale observational studies over time without intervention are better suited for evaluating long-term habitual effects. The differences among the studies highlight the diversity in research data and the varying outcomes across different study models. However, the results contributed to the meta-analysis, and no significant publication bias was observed.

The variation among individual studies was divided into two groups based on the forest plot, and an outlier analysis was conducted to assess the outlier points and their contribution weights to the combined analysis of individual studies. The analysis results indicated that the Cook's distance values for all studies were smaller than 1, suggesting no significant outliers in the meta-analysis [29]. Additionally, the contribution weights of the studies were determined, with study 6 (an intervention study) and study 16 (a longitudinal observational study) having the highest weights in the data and contributing roughly equally to the combined analysis (Table 6).

3.5. Examination of publication bias

The meta-analysis was conducted across various study groups and models, considering potential bias in sample selection and the outcomes when assessing the positive effects of tea on the human nervous system. To evaluate whether these positive results might be influenced by publication bias - where studies with favourable outcomes are more likely to be published than those with average or low effectiveness - we assumed the null hypothesis (H_0) that there is no publication bias in the studies included in the analysis. The alternative hypothesis (H_1) was then formulated to test against H_0. To assess the presence of publication bias, we employed a funnel plot (Fig. 4).

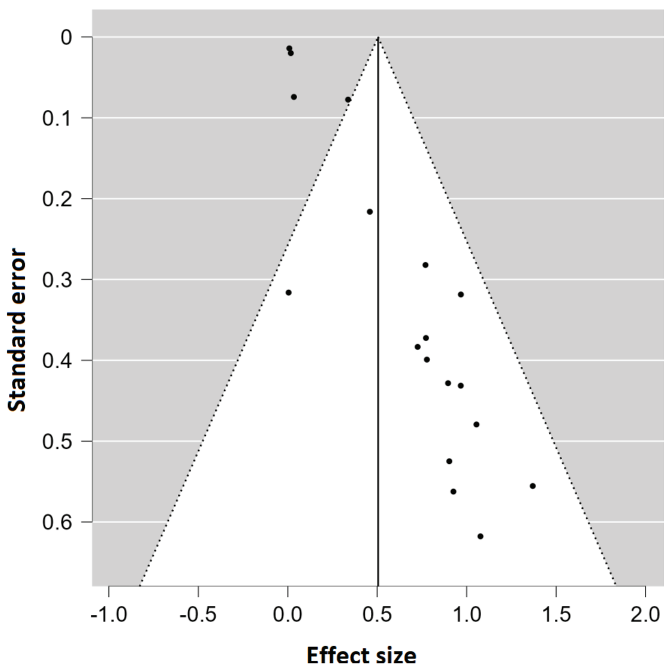

Fig. 4. Funnel plot representing publication bias in the meta-analysis.

Table 7. Statistical test result for publication bias.

	Kendall's τ	p
Rank test	0.137	0.454

The funnel plot shows that publications tend to cluster towards the right of the vertical axis. However, the majority of study outcomes still fall within the appropriate 95% confidence interval, suggesting that significant publication bias is not present. We conducted a Kendall test to further confirm the absence of publication bias in the 18 studies included in the meta-analysis (Kendall's τ) (Table 7). The result of this test yielded $\tau=0.137$ and $p=0.454$, indicating that there is insufficient evidence to reject H_0 and accept H_1. Thus, the studies analysed in this meta-analysis do not exhibit significant publication bias [30]. In summary, the analysis suggests that no significant publication bias affects this meta-analysis's results, ensuring the reliability of the synthesised findings.

4. Conclusions

This analysis was conducted to examine and confirm the positive effects of tea and its extracted compounds on the human nervous system. The selected studies displayed diversity in research methods and evaluation criteria, which helped reaffirm the initial hypotheses. The results from this comprehensive analysis can serve as a valuable source of information in the development of herbal products and provide a foundation for future studies using tea and its extracted compounds as positive controls.

However, it is essential to note that this analysis primarily focused on positive effects and did not fully explore potential adverse effects or hazards. This highlights the need for further in-depth research using diverse models to comprehensively evaluate tea's effects and its extracted compounds. Specifically, clinical trials and additional experiments are required to identify any adverse effects and non-positive impacts that tea might have. Therefore, this analysis can be considered an initial step in understanding and assessing the properties of tea and its extracted compounds. However, a considerable amount of work remains to gain a comprehensive and objective perspective on this topic.

CRediT author statement

Quoc Dang Quan: Methodology, Formal analysis, Original draft preparation, Visualisation; Tuan Loc Le: Investigation, Data curation, Writing; Tran Minh Ly Nguyen: Conceptualisation, Data curation, Investigation; Thanh Cong Nguyen: Investigation, Data curation, Formal analysis; My Ngoc Bui: Investigation, Data curation, Visualisation; Hoang Dung Tran: Supervision, Validation, Writing - Reviewing and Editing.

COMPETING INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this article.

REFERENCES

[1] N. Miyoshi, M. Pervin, T. Suzuki, et al. (2015), "Green tea catechins for well-being and therapy: Prospects and opportunities", *Botanics: Targets and Therapy*, **5**, pp.85-96, DOI: 10.2147/BTAT.S91784.

[2] T. Suzuki, M. Pervin, S. Goto, et al. (2016a), "Beneficial effects of tea and the green tea catechin epigallocatechin-3-gallate on obesity", *Molecules*, **21(10)**, 1305, DOI: 10.3390/molecules21101305.

[3] T. Suzuki, S. Hayakawa, S. Imai, et al. (2016b), "Health benefits of tea consumption", *Beverage Impacts on Health and Nutrition: Second Edition*, *Humana Cham*, pp.49-67.

[4] D.G. Nagle, D. Ferreira, Y.D. Zhou, et al. (2006), "Epigallocatechin-3-gallate (EGCG): Chemical and biomedical perspectives", *Phytochemistry*, **67(17)**, pp.1849-1855, DOI: 10.1016/j.phytochem.2006.06.020.

[5] S.Q. Chen, Z.S. Wang, Y.X. Ma, et al. (2018), "Neuroprotective effects and mechanisms of tea bioactive components in neurodegenerative diseases", *Molecules*, **23(3)**, DOI: 10.3390/molecules23030512.

[6] A. Schmidt, F. Hammann, B. Wölnerhanssen, et al. (2014), "Green tea extract enhances parieto-frontal connectivity during working memory processing", *Psychopharmacology*, **231(19)**, pp.3879-3888, DOI: 10.1007/s00213-014-3526-1.

[7] A. Scholey, L.A. Downey, J. Ciorciari, et al. (2012), "Acute neurocognitive effects of epigallocatechin gallate (EGCG)", *Appetite*, **58(2)**, pp.767-770, DOI: 10.1016/j.appet.2011.11.016.

[8] E.L. Wightman, C.F. Haskell, J.S. Forster, et al. (2012), "Epigallocatechin gallate, cerebral blood flow parameters, cognitive performance and mood in healthy humans: A double-blind, placebo-controlled, crossover investigation", *Human Psychopharmacology: Clinical and Experimental*, **27(2)**, pp.177-186, DOI: 10.1002/hup.1263.

[9] M. Ota, C. Wakabayashi, J. Matsuo, et al. (2014), "Effect of L-theanine on sensorimotor gating in healthy human subjects", *Psychiatry and Clinical Neurosciences*, **68(5)**, pp.337-343, DOI: 10.1111/pcn.12134.

[10] A. Yoto, M. Motoki, S. Murao, et al. (2012), "Effects of L-theanine or caffeine intake on changes in blood pressure under physical and psychological stresses", *Journal of Physiological Anthropology*, **31(1)**, pp.1-9, DOI: 10.1186/1880-6805-31-28.

[11] T. Giesbrecht, J.A. Rycroft, M.J. Rowson, et al. (2010), "The combination of L-theanine and caffeine improves cognitive performance and increases subjective alertness", *Nutritional Neuroscience*, **13(6)**, pp.283-290, DOI: 10.1179/147683010X12611460764840.

[12] S.J. Einöther, V.E. Martens, J.A. Rycroft, et al. (2010), "L-theanine and caffeine improve task switching but not intersensory attention or subjective alertness", *Appetite*, **54(2)**, pp.406-409, DOI: 10.1016/j.appet.2010.01.003.

[13] G.N. Owen, H. Parnell, E.A.D. Bruin, et al. (2008), "The combined effects of L-theanine and caffeine on cognitive performance and mood", *Nutritional Neuroscience*, **11(4)**, pp.193-198, DOI: 10.1179/147683008X301513.

[14] S.P. Kelly, M.G. Ramirez, J.L. Montesi, et al. (2008), "L-theanine and caffeine in combination affect human cognition as evidenced by oscillatory alpha-band activity and attention task performance", *The Journal of Nutrition*, **138(8)**, pp.1572S-1577S, DOI: 10.1093/jn/138.8.1572S.

[15] C.F. Haskell, D.O. Kennedy, A.L. Milne, et al. (2008), "The effects of L-theanine, caffeine and their combination on cognition and mood", *Biological Psychology*, **77(2)**, pp.113-122, DOI: 10.1016/j.biopsycho.2007.09.008.

[16] K. Kimura, M. Ozeki, L.R. Juneja, et al. (2007), "L-theanine reduces psychological and physiological stress responses", *Biological Psychology*, **74(1)**, pp.39-45, DOI: 10.1016/j.biopsycho.2006.06.006.

[17] S.K. Park, I.C. Jung, W.K. Lee, et al. (2011), "A combination of green tea extract and l-theanine improves memory and attention in subjects with mild cognitive impairment: A double-blind placebo-controlled study", *Journal of Medicinal Food*, **14(4)**, pp.334-343, DOI: 10.1089/jmf.2009.1374.

[18] M.S. Ritsner, C. Miodownik, Y. Ratner, et al. (2010), "L-theanine relieves positive, activation, and anxiety symptoms in patients with schizophrenia and schizoaffective disorder: An 8-week, randomized, double-blind, placebo-controlled, 2-center study", *The Journal of Clinical Psychiatry*, **72(1)**, pp.34-42, DOI: 10.4088/JCP.09m05324gre.

[19] A.L. Brown, J. Lane, J. Coverly, et al. (2008), "Effects of dietary supplementation with the green tea polyphenol epigallocatechin-3-gallate on insulin resistance and associated metabolic risk factors: Randomized controlled trial", *British Journal of Nutrition*, **101(6)**, pp.886-894, DOI: 10.1017/S0007114508047727.

[20] Y. Tomata, M. Kakizaki, N. Nakaya, et al. (2012), "Green tea consumption and the risk of incident functional disability in elderly Japanese: The Ohsaki Cohort 2006 study", *The American Journal of Clinical Nutrition*, **95(3)**, pp.732-739, DOI: 10.3945/ajcn.111.023200.

[21] L. Feng, X.I.N.Y. Gwee, E.H. Kua, et al. (2010), "Cognitive function and tea consumption in community-dwelling older Chinese in Singapore", *The Journal of Nutrition, Health & Aging*, **14**, pp.433-438, DOI: 10.1007/s12603-010-0095-9.

[22] A. Hozawa, S. Kuriyama, N. Nakaya, et al. (2009), "Green tea consumption is associated with lower psychological distress in a general population: The Ohsaki cohort 2006 study", *The American Journal of Clinical Nutrition*, **90(5)**, pp.1390-1396, DOI: 10.3945/ajcn.2009.28214.

[23] S. Kuriyama, A. Hozawa, K. Ohmori, et al. (2006), "Green tea consumption and cognitive function: A cross-sectional study from the Tsurugaya Project", *The American Journal of Clinical Nutrition*, **83(2)**, pp.355-361, DOI: 10.1093/ajcn/83.2.355.

[24] G.M. Sullivan, R. Feinn (2012), "Using effect size-or why the P value is not enough", *Journal of Graduate Medical Education*, **4(3)**, pp.279-282, DOI: 10.4300/JGME-D-12-00156.1.

[25] J. Hönekopp, A.H. Linden (2022), "Heterogeneity estimates in a biased world", *PLOS ONE*, **17(2)**, DOI: 10.1371/journal.pone.0262809.

[26] Y. Dodge (2006), *The Oxford Dictionary of Statistical Terms*, Oxford [Oxfordshire]: Oxford University Press, 508pp.

[27] J.P. Higgins, S.G. Thompson, J.J. Deeks, et al. (2003), "Measuring inconsistency in meta-analyses", *BMJ*, **327(7414)**, pp.557-560, DOI: 10.1136/bmj.327.7414.557.

[28] A.G. Lalkhen, A. McCluskey (2008), "Statistics V: Introduction to clinical trials and systematic reviews", *Continuing Education in Anaesthesia, Critical Care & Pain*, **8(4)**, pp.143-146, DOI: 10.1093/bjaceaccp/mkn023.

[29] R.D. Cook (1979), "Influential observations in linear regression", *Journal of The American Statistical Association*, **74(365)**, pp.169-174, DOI: 10.2307/2286747.

[30] C.B. Begg, M. Mazumdar (1994), "Operating characteristics of a rank correlation test for publication bias", *Biometrics*, **50(4)**, pp.1088-1101.