Chicken Essence and Cognitive Function: A Systematic Review and Meta-Analysis

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Objective: *To determine the efficacy of chicken essence for improving cognitive performance.*
Material and Method: *English language database including Embase, Medline, PsychINFO and Global Health (up to May 2014) were searched. Inclusion criteria were randomized double-blind controlled studies (RCT) or cross-over studies comparing chicken essence with placebo.*
Results: *Four trials were included. Three studies measured cognitive performance, while the remaining study assessed cognitive performance after fatigue-inducing tasks. When compared to placebo, chicken essence improved arithmetic (SMD -1.23, 95% CI -2.51 to -0.31) and memory (SMD -3.94, 95% CI -4.59 to -3.29). There were no ascertainable positive effects on attention/concentration (SMD -1.55, 95% CI -4.77 to 1.67), anti-fatigue (SMD 1.20, 95% CI 0.53 to 1.88), and recovery from mental fatigue (SMD -0.38, 95% CI -1.0 to 0.25). However, the levels of evidence with respect to each cognitive domain was rated as 'very low' using the GRADE system because of low sample size, inconsistency and high risk of bias.*
Conclusion: *There are few trials examining the efficacy of chicken essence to cognitive performance. Furthermore, the level of evidence was very low. Using it for this indication is not suggested at present. Additional high quality RCT designs are needed to arrive at a stronger conclusion.*

Keywords: *Chicken essence, Chicken extract, Cognition, Complementary therapies*

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Essence of chicken is an aqueous extract of chicken meat with a long history of consumption, particularly in China and Southeast Asia. It was claimed as a traditional remedy for a variety conditions including 1) helping the body to recover from fatigue or illness, 2) strengthening athletes, 3) recovery from mental fatigue, and 4) stimulating and promoting cognitive performance[1,2]. In the last decade, there has been a revival of interest in traditional remedies. Although the mechanisms of action of chicken essence remain largely unknown, there are now some studies that examine the efficacy of chicken essence on cognitive function. However, no systematic review has yet been conducted on the topic. Therefore, this review aimed to study the efficacy of chicken essence on cognitive function when compared to placebos in the healthy population.

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Material and Method

Information sources and search methods

Information were obtained through databases including Embase (1980-May 2014), Medline (1946-May 2014), PsychINFO (1806-May 2014), and Global Health (1973-May 2014). Search terms used consisted of "chicken essence" and "chicken extract" with the limits "English language". The search methods were independently conducted by two researchers (TC and KP). Additional searches were conducted with other sources including electronic abstracts, Google Scholar, ClinicalTrials.gov, results of studies that are dispersed on websites of companies manufacturing various brands of chicken essence, and references of the included studies. We also directly contacted manufacturing companies to inquire research results.

Inclusion criteria

1) Randomized controlled trials or cross-over trials.

2) Participants were from a healthy population.

3) Study outcome comparing chicken essence and placebo.

4) Study outcome were cognitive performance or mental fatigue.

Data collection and analysis

Data extraction and evaluation of risk of bias were conducted by the two authors (TC and KJ). Risk of bias was evaluated by the Cochrane Collaboration method.

Study results were combined by the random-effect model as the results had heterogeneity. Statistical heterogeneity was assessed using the Q-test and I^2 statistics. All analyses were performed using Open Meta [Analyst] program. It was found that most studies evaluated neuropsychological tests for various aspects of cognitive functions; we analyzed each aspect separately. When multiple measures were used to assess a single cognitive domain, we selected scores on one assessment that we determined as most commonly used or most clinical sound. The evaluation of level of evidence was conducted by the GRADE System[3].

Results

Search results

Searches of electronic databases yielded 56 studies. Two additional studies were found from other sources. After reading abstracts, 25 studies were excluded on the ground of irrelevance, leaving seven full-text studies to be evaluated. Thereafter, three studies were excluded (Table 1). Finally, there were four studies included in this review. Search results were displayed in Fig. 1.

Study characteristics

The characteristics of the included studies are presented in Table 2. Data extraction and evaluation of the studies were conducted by TC and KJ.

Study design

Three studies were randomized double-blind placebo controlled design (Azhar, 2003, 2008, 2013) and the other study was a placebo-controlled crossover study (Yamano, 2013).

Participants

In the study by Azhar (2003), participants included 176 fourth-year medical students, both male and female, between the age of 23 and 24. At the end of the study, there were 56 participants in the chicken essence group and 52 in the placebo group. Azhar (2008) participants included 102 fourth-year medical students between the age of 22 and 24. At the end of the study there were 69 participants. There were 38 participants in the chicken essence group and 31 subjects in the placebo group. In Yamano (2013), 20 male participants had the mean age of 34.7 ± 0.83, with no subjects leaving the study before it was completed. In the study by Azhar (2013), there were 46 participants, both male and female, with a mean age of 47.5. There were 20 participants remaining at the end of the study, which were divided into 10 participants in the experimental group and 10 participants in the control group.

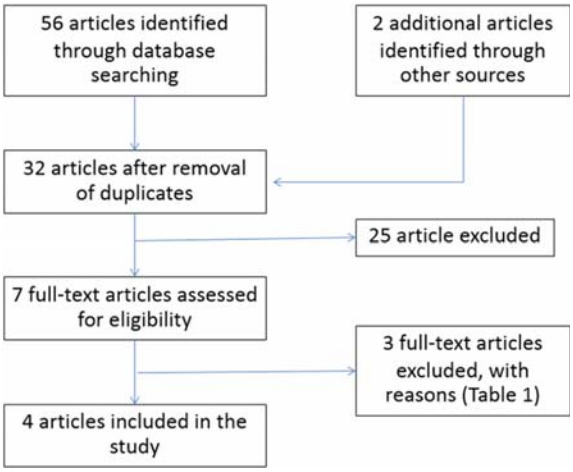

Fig. 1 Flow chart of study selection.

Table 1. Studies that were excluded

Studies	Rationale
Azhar, 2001[4]	Participants were patients with anxiety disorders. Outcomes were improvements from anxiety disorders.
Shin, 2007[5]	Intervention is an extract comprising various nutrients including capsaicin, green tea, and chicken essence. The outcomes were the measure of autonomic nervous activities.
Nagai, 1996[2]	This was a cross-over study, but without randomization, and the study did not present the baseline data.

Table 2. Characteristics of included studies [sorted by year]

Study	Study design	Duration	Participants*	Intervention	Outcome
Azhar, 2003[5]	Randomized double-blind placebo controlled design	14 days	108 male and female medical students, age: 23-24 years	1) Placebo (water with caramel) 2) Essence of Chicken 70 ml/day 3) Carageenan protein drink 70 ml/day	1) Cognitive performance 2) Mental well-being 3) Physical well-being
Azhar, 2008[6]	Randomized double-blind placebo controlled design	14 days	69 male and female medical students, age 22-24 years	1) Placebo (water with milk protein) 2) Essence of chicken 70 ml/day	1) Cognitive performance 2) Stress 3) EEG
Yamano, 2013[7]	Placebo-controlled crossover study	4 weeks	20 healthy males, age: 34.7±0.8 years	1) Placebo (water with milk casein and caramel) 2) Brand's Essence of Chicken 140 ml/day	1) Cognitive performance after fatigue-inducing task 2. Subjective feeling of fatigue
Azhar, 2013[8]	Randomized double-blind placebo controlled design	6 weeks	20 males and females, age: 35-65 years	1) Placebo 2) Chicken extract (Chicken meat ingredient-168) 670 mg/day	1) Cognitive performance

* The number of participants at the end of the study

Interventions

In Azhar, 2003 and 2008, 70 ml of liquid chicken essence were administered per day. In the study by Yamano (2013), 140 ml of liquid chicken essence were administered per day. Only the study by Azhar (2013) used a 670-mg tablet of chicken extract (chicken meat ingredient-168; CMI-168).

Outcomes

All studies measured cognitive performance, whereby the domains of cognition tested differed. We divided them into three domains (Table 3). Only the study by Yamano (2013) measured cognitive performance after a task inducing mental fatigue.

Risk of bias in included studies

The risk of bias of all included studies was evaluated by the Cochrane Collaboration method (Table 4).

Random sequence generation and allocation concealment

None of the four studies presented the details of the randomization and did not explain the method of concealment.

Blinding

Blinding participants was a challenge for studies that utilized liquid essence of chicken as it has a distinct color, smell, and taste. Even though placebo samples (made mainly of gelatin and caramel) had similar color and external characteristics, the smell and taste may noticeably different from the real essence of chicken. Therefore, there was a high probability that participants would be aware of whether the doses they were given were real essence of chicken or placebos. However, we were aware that this was a limitation to studying this type of intervention. In the study by Azhar (2013), tablet-form chicken essence was given to subjects without descriptions of whether or not the tablets were similar or not between the placebo and chicken essence groups. In terms of blinding among other persons in the studies, only the study by Azhar (2013) had clear descriptions. Other studies did not indicate the blinding process among other personnel. Assessors in the studies by Azhar 2003, 2008, and 2013 were all blinded; the exception was the study by Yamano in 2013, which did not discuss any form of blinding.

Incomplete outcome data

The authors considered the outcomes of the study by Azhar in 2008 unclear because there were 25 subjects who were excluded from the study due to 'technical errors', and there were no details on the missing data. Azhar (2013) was considered high risk, as 26 out of the 46 subjects discontinued the study

Table 3. Cognitive domains measured in each study

Study	Attention/concentration	Memory	Arithmetic
Azhar, 2003	Digit span	Figures construction, three-minute memory test	Mental arithmetic test
Azhar, 2008	Digit span, Letter-number sequencing		Arithmetic test (from subtest of the WAIS-III)
Azhar, 2013	Digit span, letter-number sequencing	Rey Auditory Verbal Learning test (RAVLT)	

Table 4. Risk of bias in included studies

Risk of bias	Azhar 2003	Azhar 2008	Yamano 2013	Azhar 2013
Random sequence generation	Unclear	Unclear	Unclear	Unclear
Allocation concealment	Unclear	Unclear	Unclear	Unclear
Blinding of participants and personnel	High risk	High risk	High risk	Unclear
Blinding of outcome assessment	Low risk	Low risk	Unclear	Low risk
Incomplete outcome data	Low risk	Unclear	Low risk	High risk
Selective reporting	Low risk	Low risk	High risk	High risk
Other sources of bias	Low risk	Low risk	Low risk	Low risk

(56.5%), and the analysis of only the remaining 20 subjects were reported.

Selective reporting

Azhar (2013) did not present the mean and SD of the scores of cognitive function. Only figures and *p*-values were reported, therefore, they could not be entered into a meta-analysis. The study by Yamano in 2013 showed outcomes comprising three assessments which measured the same factor. Measurements were conducted twice, immediately after fatigue-inducing tasks and again 60 minutes after rest. This contributed to the study having a large number of outcomes. In addition, the study also presented only the changes in the before- and after-scores in each group (intragroup) without comparing the data between the control group and the intervention group (between group analysis).

Funding and conflict of interest

Azhar, 2003 and 2008 did not report about funding and conflict of interest. Azhar (2008) indicated in the method of research that the chicken essence and placebo were sponsored by a private company (anonymous). The study by Yamano in 2013 was sponsored by Cerebos Pacific Ltd. through Suntory Holdings Ltd. One of the researchers (out of a total of 6) worked with Suntory Holding Ltd., and another researcher worked with Cerebos Pacific Ltd. The study by Ashar (2013) was sponsored by Cerebos Pacific Ltd., in which two out of the five researchers worked with Cerebos Pacific Ltd.

Efficacy of interventions

Attention and concentration

There were three studies that evaluated attention and concentration including the studies by Azhar 2003, 2008, and 2013. The study by Azhar (2003) measured the digit span, whereas the study by Azhar 2008 and 2013 measured the digit span and letter-number sequencing.

In the study by Azhar in 2003, the increase in digit span scores of the placebo group was 1.02$\pm$0.41 points, while the chicken essence group was 2.5$\pm$0.5, which has statistically significant differences (p<0.05).

The results of the study by Azhar (2008) reported on the analysis of a comparison between the scores of the post-test of the chicken essence and placebo groups. A statistically significant difference was found only for the scores for letter-number sequencing (chicken essence 13.55$\pm$0.41, placebo 12.1$\pm$0.44, t = 2.4, p<0.05). There was no statistically significant difference detected in the digit forward and digit backward scores between the two groups (digit forward: chicken essence 11.26$\pm$3.27, placebo 11.45$\pm$0.39, t = 0.35, p>0.05; digit backward: chicken essence 8.39$\pm$0.36, placebo 8.61$\pm$0.36, t = 0.42, p>0.05).

The study by Azhar 2013 found that post-test scores in the 6th week for the subject group that received chicken essence had better digit span backward and letter-number sequencing scores than the placebo group with statistical significance (p<0.01 and p<0.001, respectively). The study did not report on the mean and SD.

We analyzed the overall attention and concentration outcomes of the chicken essence of two studies using the digit span scores of the study by Azhar 2003 and 2008, which found that the scores for the chicken essence group had no statistically significant differences from the scores of the placebo group. The standardized mean difference (SMD) was -1.55 (95% CI -4.77 to 1.67, p = 0.35), and there was heterogeneity with statistical significance (Q = 75.51, df = 1, p<0.001; I^2 99%).

Memory

Azhar (2003) evaluated memory with the figures construction test and the three-minute memory test. The outcomes of the figures construction tests found that the scores of the placebo group increased by 0.42$\pm$0.11, whereas the scores of the chicken essence subjects group increased by 0.68$\pm$0.14, which had no statistically significant difference (p = 0.21). The scores of the 3-minute memory tests found that the scores of the placebo group improved by 0.19$\pm$0.1, while the scores for the chicken essence group increased 0.63$\pm$0.12, which were different with statistical significance (p<0.01), with SMD = -3.94 (95% CI -4.59 to -3.29).

The study by Azhar (2013) found that the RAVLT scores of the group that received the CMI-168 were better than the scores of the placebo group with statistical significance p<0.001 in all 5 sub-tests including the immediate memory, new verbal learning, susceptibility to interference, retention of information after a period of time, and memory recognition tests. However, the study did not report the mean and SD.

Arithmetic

Azhar (2003), the Mental Arithmetic Test (MAT) scores of the placebo group increased by 0.65$\pm$0.17 points, while the scores of the chicken

essence subject group increased by 1.63±0.28 points, which had no statistically significant differences (p<0.05). The study by Azhar (2008) reported that the post-test arithmetic scores between the two groups had no statistically significant differences (chicken essence 14.89±0.64, placebo 15.74±0.84, t = 0.81, p>0.05).

The combined result in the arithmetic performance were analyzed in the two studies by Azhar 2003 and 2008, which found that the chicken essence group had better scores than the placebo group with statistical significance with the standardized mean difference (SMD) = -1.23 (95% CI -2.15 to -0.31, p = 0.009). There was statistically significant heterogeneity (Q = 13.88, df = 1, p<0.001; I^2 = 93%).

Cognitive performance after fatigue-inducing task

Only the study done by Yamano in 2013 examined the cognitive task after the participants completed the fatigue-inducing task. The outcome of the study was reaction time from three experiments including Task A, where by subjects were to press the button on the right if they saw a blue light and the button on the left if they saw a red light; Task B, mismatching the color of traffic lights with Japanese characters (Stroop trials), and Task C, matching the color of traffic lights with Japanese characters (non-Stroop trials). Assessments were conducted three times including the first day of the study, the first week, and the fourth week. Two evaluations are done per day including after the fatigue-inducing task (to see the anti-fatigue effect) and again after a 60-minute rest (to see fatigue recovery effect). However, this study chose to present only the intragroup difference (which compares the before and after scores of each group, without comparing between groups). We used only data from the end of the fourth week, without using the data from the first week, and used the Task B (Stroop trial) as the main representation of the study.

In terms of the ability to reduce fatigue after work, the study found that the reaction time of the measurement taken immediately after a fatigue-inducing task, when compared to the score from the baseline in the chicken essence group, had no statistically significant difference in all three sub-tests. We calculated the SMD from the Task B test which found that the group that received the chicken essence had longer reaction time when compared to the control group, SMD 1.20 (95% CI 0.53 to 1.88).

The reaction time after a 60-minute rest in the chicken essence group for Task A did not have any statistically significant different before and after receiving the chicken essence (p>0.05). However, the reaction time after Task B and C found that, the reaction times improved with statistical significance from the baseline (p>0.05 in both tests). The authors calculated the SMD for task B, which found that SMD was -0.38 (95% CI -1.0 to 0.25).

Level of evidence

Level of evidence of each outcome of study

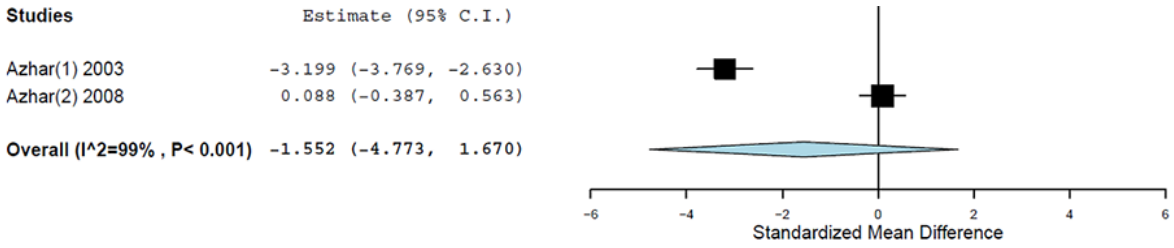

Fig. 2 Forest plot of the efficacy of chicken essence on attention and concentration.

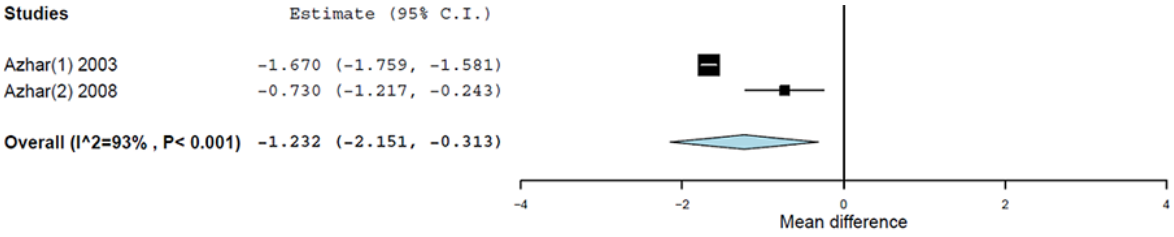

Fig. 3 Forest plot of the efficacy of chicken essence on arithmetic performance.

using the GRADE is displayed in Table 5.

Publication bias

As there were a limited number of studies, it was not possible to conduct a funnel plot.

Discussion

The goal of this study was to review and examine the quantitative evidence of chicken essence and cognitive performance. To the authors' knowledge, this is the first systematic review examining this issue. The results of this review demonstrated that there were only few RCT that studied the effects of chicken essence on cognitive performance, most of which were small studies. Two studies (Yamano, 2013 and Azhar, 2013) involved less than 30 participants. By the end of the four studies, there were only 217 participants. Furthermore, all studies had problematic outcome reports because they did not follow the CONSORT guideline. This led to a large amount of unclear data, which affected the quality of the studies. In addition, only the studies by Azhar 2003 and 2008 presented sufficient data to be used in the meta-analysis. However, there was heterogeneity between the two studies.

Cognitive performance after fatigue-inducing task

Only the study done by Yamano in 2013 had the objective of measuring this outcome. However, it should be mentioned that the researchers chose to present only the intragroup difference, without presenting the between group difference which, in our opinion, was the main outcome of the study. The study found that there was no statistically significant differences in the anti-fatigue effect before and after receiving chicken essence in all three tests, which showed that chicken essence does not have an effect on reducing mental fatigue. The tests conducted after resting to measure recovery from fatigue found that the group that received chicken essence had improved response times in two out of three measures. However, when we calculated the SMD of Task B comparing the scores of the chicken essence and control groups, there was no significant difference between the two groups. Therefore, it should not be claimed that chicken essence is more effective than placebo.

Memory

There were two studies that studied memory. The study by Azhar in 2003 found that there was inconsistency as the figures construction test demonstrated that there was no statistically significant difference between the two groups. However, the 3-minute memory test showed that the group that received chicken essence scored better than the placebo group. Meanwhile, the study by Azhar in 2013 that conducted the RAVLT test found that the chicken essence group

Table 5. Level of evidence

Outcomes	SMD (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
Attention/concentration	-1.55 (-4.77 to 1.67)	177 (2 studies)	⊕OOO Very low*
Memory	-3.94 (-4.59 to -3.29)	108 (1 study)	⊕OOO Very low**
Arithmetic	-1.23 (-2.15 to -0.31)	177 (2 studies)	⊕OOO Very low***
Cognitive performance after fatigue-inducing task	1.20 (0.53 to 1.88)	20 (1 study)	⊕OOO Very low****
Rest session	-0.38 (-1.0 to 0.25)		

Very low = true effect is likely to be substantially different from the estimate of effect

* Risk of bias assessment: considered serious as there was unclear data or risk of bias in various aspects; inconsistency: considered serious as there is unexplained heterogeneity of results, the two studies that are included in the results had very different SMD scores; imprecision: considered serious as the sample size was very small.

** Risk of bias assessment: considered serious as there was unclear data or risk of bias in various aspects; inconsistency: considered serious as there was only one study with conflicting results; imprecision: considered serious as the sample size was very small.

*** Risk of bias assessment: considered serious as there was unclear data or risk of bias in many aspects; imprecision: considered serious as the sample size was very small.

**** Risk of bias assessment: considered serious as there was unclear data or risk of bias in many aspects; inconsistency: considered serious as there was only one study and the outcome of each evaluation method were inconsistency; imprecision: considered serious as the sample size was very small.

scored better than the placebo group with statistical significance in all sub-scores of RAVLT.

Meta-analysis

Only data on attention and concentration and arithmetic were sufficient for meta-analysis. In terms of attention and concentration, there was no statistically significant differences in the combined result between the chicken essence and control groups with SMD -1.55 (95% CI -4.77 to 1.67, $p>0.05$). As for arithmetic, it was found that the chicken essence group scored better than the placebo group with statistical significance with SMD -1.23 (95% CI -2.15 to -0.313, $p<0.05$).

Level of evidence

The most important factor to be considered is the level of evidence. An analysis found that the level of evidence using the GRADE system in all four aspects of cognitive performance were 'very low'. This means that the real effectiveness may be different from the results of the study. The main reasons were that sample sizes were small, there was a risk of bias, and there was heterogeneity between the studies. Therefore, it should not be concluded with support that chicken essence is effective in enhancing cognitive performance.

Conclusion

The outcome on the efficacy of chicken essence to enhance cognitive function and prevention of fatigue did not present sufficient evidence to conclude that it has any benefits. As there was a very low level of evidence, and uncertainty remained in the studies' results. As such, it is not recommended to use chicken essence for indications claiming that it can improve cognitive performance. The efficacy of chicken essence requires further high-quality RCT studies in arriving at a stronger conclusion.

Contribution

Thammanard Charernboon designed the study, searched and assessed the articles, analyzed the data, and wrote the manuscript. Kankamol Jaisin assessed the articles and assisted with writing the manuscript. Kerrati Pattanaseri searched the articles and assisted with writing the manuscript. All authors have approved the final manuscript.

What is already known on this topic?

Chicken essence is widely used for its potential effects on cognitive performance. To date, no systematic review has been conducted on this topic.

What this study adds?

There is no convincing evidence from this review that demonstrated chicken essence can improve cognitive performance.

Acknowledgements

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Potential conflicts of interest

None.

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ซุปไก่สกัดกับการทำงานของสมอง: การทบทวนวรรณกรรมอย่างเป็นระบบและการวิเคราะห์อภิมาน

ธรรมนาถ เจริญบุญ, กันต์กมล จัยสิน, กีรติ พัฒนเสรี

ภูมิหลัง: *เพื่อศึกษาถึงประสิทธิภาพของซุปไก่สกัดต่อการทำงานของสมอง (cognitive performance)*

วัสดุและวิธีการ: *ทำการสืบค้นฐานข้อมูล Embase, Medline, PsychINFO และ Global Health (ถึงเดือนเมษายน พ.ศ. 2557) เกณฑ์การคัดเลือกงานวิจัย ได้แก่ เป็นการศึกษาเชิงทดลองแบบสุ่มและมีกลุ่มควบคุม หรือการศึกษาแบบ cross-over ที่เปรียบเทียบระหว่างซุปไก่สกัดกับ placebo*

ผลการศึกษา: *พบว่ามีสี่การศึกษาที่เข้าเกณฑ์การคัดเลือก ในจำนวนนี้มีสามการศึกษาที่ทำการศึกษาเรื่องประสิทธิภาพการทำงานของสมอง (cognitive performance) ในขณะที่อีกหนึ่งการศึกษาทำการวัดเรื่องการทำงานของสมองภายหลังจากทำให้เกิดความเหนื่อยล้า ประสิทธิภาพของซุปไก่สกัดเมื่อเปรียบเทียบกับยาหลอก พบว่าซุปไก่สกัดเพิ่มความสามารถคณิตศาสตร์ (SMD -1.23, 95% CI -2.51 to -0.31) และความจำ (SMD -3.94, 95% CI -4.77 to 3.29) ในขณะที่ไม่พบประสิทธิภาพในด้านสมาธิ (SMD -1.55, 95% CI -4.77 to 1.67) การต่อต้านความเหนื่อยล้า (SMD 1.20, 95% CI 0.53 to 1.88) และการฟื้นฟูจากความเหนื่อยล้า (SMD -0.38, 95% CI -1.0 to 0.25) แต่อย่างไรก็ตามพบว่าระดับความเชื่อมั่นของหลักฐาน (level of evidence) เมื่อประเมินด้วย GRADE system อยู่ในระดับ "ต่ำมาก" ในทุกด้าน เนื่องจากกลุ่มตัวอย่างมีจำนวนน้อย ผลการศึกษามีความไม่แน่นอน และการศึกษามี risk of bias ที่สูง*

สรุป: *มีงานวิจัยจำนวนไม่มากที่ศึกษาถึงประสิทธิภาพของซุปไก่กับการทำงานของสมอง โดยมีระดับความเชื่อมั่นของหลักฐานอยู่ในเกณฑ์ที่ต่ำมาก ดังนั้นจึงยังไม่แนะนำให้ใช้ซุปไก่สกัดเพื่อข้อบ่งใช้เหล่านี้ การศึกษาเพิ่มเติมโดยใช้การทดลองแบบสุ่มและมีกลุ่มควบคุมที่มีคุณภาพเป็นสิ่งที่จำเป็นเพื่อที่จะได้ข้อสรุปที่ชัดเจนยิ่งขึ้น*