



DOSSIER · SUBSTANCE

Theacrine

Theacrine is a **purine alkaloid** derived from the tea plant *Camellia kucha* that has been investigated in controlled human trials since 2015. Research focuses on **fatigue** and **cognitive performance**, but also provides early indications of **cardiovascular effects**. The evidence base is young but methodologically broad, comprising nine controlled human studies.

21

STUDIES IN
TOTAL

11

IN HUMANS

9

OF WHICH
CONTROLLED

0

IN ANIMALS

0

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Theacrine at a Glance

ORIGIN:

Theacrine is a naturally occurring purine alkaloid (1,3,7,9-tetramethyluric acid) derived from the leaves of the tea plant *Camellia kucha*, a variety native to southern China. Traditionally consumed as 'Kucha tea', it is structurally related to caffeine but exhibits a longer half-life and is not metabolised by the enzyme CYP1A2. Its primary mechanism of action involves adenosine receptors and modulation of neurotransmitters such as dopamine and noradrenaline, though with a delayed and prolonged profile compared to caffeine.

EVIDENCE BASE:

21 reviewed papers · 9 controlled human studies · 2 observational studies · 2 reviews · 0 animal studies · 0 cell culture studies

STRONGEST EVIDENCE:

- **Fatigue & cognition:** Controlled studies show significant increases in subjective energy, focus, and concentration after theacrine intake (200–400 mg) when combined with caffeine or methylxanthine. A study in e-sports athletes demonstrated improved reaction times and inhibitory control for the combination of theacrine with other stimulants, without increased side effects compared to caffeine alone. The effects of theacrine as a monotherapy remain unclear.
- **Cardiovascular:** Combination studies with caffeine and theacrine showed no significant haemodynamic changes (e.g., blood pressure), whereas caffeine alone increased these parameters. This suggests a potential safety advantage for the combination, though data on theacrine as a monotherapy are lacking.
- **Safety & tolerability:** Eight-week safety studies with 200–300 mg theacrine showed no changes in clinical markers (blood count, liver/kidney values) or tolerance development, but dose-dependent improvements in subjective parameters such as motivation.
- **Cognitive performance:** Tactically trained participants showed improved results in tests such as anti-saccade and two-back after combining theacrine (150 mg) and caffeine (150 mg), while caffeine alone had no significant effects. The contribution of theacrine alone to these outcomes is not established.
- **Pharmacokinetics:** Combining theacrine (125 mg) with caffeine increased the maximum plasma concentration and bioavailability of theacrine without altering its half-life or interfering with caffeine metabolism.

LIMITATIONS:

- **Long-term effects:** All controlled studies examine acute or short-term effects (maximum 8 weeks). Long-term data on theacrine as a monotherapy or at high doses are entirely lacking.
- **Combination studies:** Most studies test theacrine with caffeine or methylxanthine, complicating the assessment of individual effects. Whether theacrine alone is similarly effective remains unclear.
- **Clinical biomarkers:** Preclinical evidence of anti-inflammatory or metabolic effects (e.g., NF-κB inhibition) exists, but these have not been systematically investigated in humans. Human data on inflammatory markers or metabolic parameters are missing, and the relevance of these findings for human applications is not established.

ASSESSMENT:

Theacrine is a purine alkaloid from *Camellia kucha* with a delayed, prolonged effect on energy, focus, and cognitive performance, showing synergistic effects when combined with caffeine but requiring systematic evaluation as a monotherapy.

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1. What Theacrine Is and How It Works

Theacrine (1,3,7,9-tetramethyluric acid) is a **naturally occurring purine alkaloid** structurally related to caffeine but with a longer half-life. It is extracted from the leaves of the tea plant *Camellia kucha*, a variety native to southern China traditionally consumed as 'Kucha tea'. Unlike caffeine, theacrine is not metabolised by the enzyme **CYP1A2**, which influences potential drug interactions. Its effects are mediated primarily via **adenosine receptors** and modulation of **neurotransmitters** such as dopamine and noradrenaline, though with a distinct pharmacological profile compared to caffeine.

For interpreting the studies, it is crucial to note that theacrine **does not produce acute stimulation** like caffeine but instead exhibits a **delayed and prolonged effect**. This explains why studies often evaluate it in combination with caffeine or other alkaloids such as **methylxanthine**—to assess synergistic effects. Bioavailability is high, but optimal dosing and timing remain unclear. Theacrine is frequently used in standardised preparations under the name **TeaCrine®**, enhancing comparability across studies.

2. What the Studies Show in Detail

The key human studies and major reviews—organised by application area, including population, duration, formulation, outcome measures, and results as reported in the original papers. Numbers are included only where the study explicitly reports them.

Distribution of **controlled human studies** by application area—the numbers are not additive as a single study may address multiple areas:

APPLICATION AREA	CONTROLLED STUDIES
Fatigue and stress	7

APPLICATION AREA	CONTROLLED STUDIES
Cognition and psyche	5
Cardiovascular system	5
Safety and tolerability	5
Musculoskeletal system	1
Bone and joint health	1
Immune system	1
Gut and microbiome	1

Cognition and Psyche

Evidence: A randomised, open-label dose–response study ⁽¹⁾ involving nine healthy participants examined theacrine (TeaCrine®) at doses of 200 mg and 400 mg over seven days. Subjective changes in energy, focus, and concentration were measured using a visual analogue scale (VAS) before and 1, 4, and 6 hours after intake. Both doses led to significant increases compared to baseline, with the 400 mg dose showing a trend towards stronger effects. A subsequent double-blind, placebo-controlled crossover study with 15 participants confirmed these findings for a single 200 mg dose, though no significant changes in gas exchange or haemodynamic parameters were observed.

Evidence: A double-blind, placebo-controlled crossover study ⁽⁴⁾ involving 50 male e-sports athletes compared a combination of caffeine (125 mg), Dynamine® (75 mg), and theacrine (50 mg) with caffeine alone and placebo. The combination significantly improved reaction time in the Psychomotor Vigilance Task and inhibitory control in the Flanker Test compared to baseline. Participants also reported higher alertness with the combination than with placebo, while caffeine alone more frequently caused headaches and anxiety. The study did not isolate the effects of theacrine, so the observed benefits cannot be attributed to theacrine alone.

Evidence: A study with 20 tactically trained participants ⁽⁷⁾ tested a combination of theacrine (150 mg) and caffeine (150 mg) against caffeine alone (300 mg) and placebo. After high-intensity interval training, the combination improved cognitive performance in tests such as Anti-Saccade and Two-Back, while caffeine alone showed no significant effects. As theacrine was not tested alone, the observed effects cannot be specifically attributed to it.

PLAUSIBLE A study with 19 healthy participants ⁽⁸⁾ examined high doses of theacrine (3, 6 and 9 mg/kg body weight) and found no significant changes in heart rate or blood pressure, but increased salivary cortisol levels after 120 and 180 minutes. Cognitive performance remained unchanged, indicating a possible stress-modulating effect at a physiological level without cognitive impairment. The study is the first to test theacrine without caffeine combination at high doses. **Hypothesis:** The elevated cortisol levels may indicate an adaptogenic effect relevant in chronic stress. What is missing: Long-term studies on the cognitive and psychological effects of theacrine without caffeine.

Gut and Microbiome

PLAUSIBLE A double-blind, placebo-controlled crossover study ⁽³⁾ with eight healthy adults examined the pharmacokinetic interaction between theacrine (25 mg or 125 mg) and caffeine (150 mg). The combination of 125 mg theacrine with caffeine increased the maximum plasma concentration and the area under the curve (AUC) of theacrine without affecting its half-life. Theacrine had no influence on the pharmacokinetics of caffeine or its metabolite paraxanthine. Hemodynamic parameters remained unchanged. **Hypothesis:** The increased bioavailability of theacrine in combination with caffeine may indicate competitive inhibition of metabolism, which is relevant for dosing in combination products. What is missing: Studies on the effect of theacrine on gut microbiota or intestinal barrier function.

Heart and Circulation

PROVEN A randomised, placebo-controlled study ⁽⁵⁾ with 48 tactical athletes compared caffeine (300 mg) with a combination of caffeine (150 mg), methyllicberine (100 mg) and theacrine (50 mg). While caffeine alone increased blood pressure, the combination showed no significant hemodynamic changes but improved reaction times and vigilance. The study did not test theacrine alone, so no conclusions can be drawn about its individual effects on performance or side-effect profile.

PROVEN A study with 20 elite canoe sprinters ⁽⁶⁾ compared caffeine, theacrine (dose not specified), their combination, and placebo. Caffeine significantly improved the 500-metre time (-1.872 s), while theacrine alone showed no statistically significant effects. The combination achieved smaller but significant improvements. Muscle oxygenation and anaerobic capacity remained unchanged. **Hypothesis:** Theacrine may show ergogenic effects similar to caffeine at higher doses or with prolonged intake, without its cardiac side effects. What is missing: Studies on the chronic effects of theacrine on heart rate variability or blood pressure regulation.

Bones and Joints

PLAUSIBLE A double-blind, placebo-controlled crossover study with 12 participants (40–70 years) examined NAD3®, a supplement containing theacrine among other ingredients, over seven days. After intake, selective changes in circulating stem cells were observed, particularly an increase in CD45^{dim}CD34⁺ cells (lymphoid stem cells) and CD45^{dim}CD34⁺CD309⁺ cells (vascular repair cells). Acute effects were not observed. **Hypothesis:** The *NAD3® formulation* may support tissue regeneration in the long term by modulating stem cell populations. What is missing: Studies on the effect of theacrine alone on bone metabolism markers or joint health.

Inflammation

PLAUSIBLE An eight-week safety study ⁽¹¹⁾ with 60 healthy participants compared placebo with 200 mg and 300 mg theacrine (TeaCrine®). Clinical safety markers (blood count, liver/kidney values, lipid profile) remained unchanged, and there were no signs of tolerance development. Subjective parameters such as energy and motivation improved in a dose-dependent manner. **Hypothesis:** Anti-inflammatory effects observed in preclinical studies may be due to inhibition of pro-inflammatory signalling pathways, which could be relevant for chronic inflammation. What is missing: Human studies with inflammatory markers such as CRP or cytokines under the influence of theacrine.

PLAUSIBLE A review article ⁽¹³⁾ summarises preclinical data on theacrine, including antioxidant and anti-inflammatory effects, such as inhibition of NF-κB activation in cell models. In addition, locomotor activation and fatigue reduction were described in animal studies. **Hypothesis:** The structural similarity to caffeine suggests that theacrine may exert anti-inflammatory effects via adenosinergic receptors. What is missing: Clinical studies on the effect of theacrine on inflammatory parameters in healthy or diseased populations; the described effects are currently limited to preclinical findings and have not been investigated in humans.

Metabolism

PLAUSIBLE A metabolomic analysis ⁽¹⁴⁾ of kucha white tea (rich in theacrine) identified 601 differential metabolites compared to conventional teas. Theacrine was enriched at ~30 mg/g in kucha tea, while caffeine and catechins were reduced. Bitter substances such as theophylline, theobromine and L-arginine were also elevated. **Hypothesis:** Theacrine may influence metabolic pathways, such as purine metabolism or mitochondrial function, though human studies on clinical metabolic parameters (e.g., glucose tolerance or lipid profile) are still missing.

Overall Picture

In controlled human studies, combinations of theacrine with caffeine or other purine alkaloids have shown consistent effects on subjective parameters such as energy, focus, and motivation. Cognitive improvements (reaction time, inhibitory control) have been observed in e-sport and tactical populations under these conditions, while ergogenic effects in sport appear less pronounced than with caffeine alone. Hemodynamic parameters remain stable under theacrine, even at high doses, indicating a favourable safety profile for the combinations tested.

The evidence base for long-term or specific physiological effects (e.g., inflammation, metabolism, stem cell modulation) is still limited. Most studies investigate acute or short-term effects, often in combination with caffeine. Preclinical data suggest potential anti-inflammatory and metabolic effects, but these remain untested in human studies. What is missing: Long-term studies on theacrine as a single substance in various populations (e.g., older adults, patients with chronic stress).

Methodology of the evidence base

[The studies on theacrine predominantly include randomised, double-blind, placebo-controlled crossover designs with 8–60 participants. Typical endpoints are subjective scales (VAS), cognitive tests (e.g., Flanker test, Psychomotor Vigilance Task), hemodynamic parameters and performance measurements (e.g., time trials, strength tests). The duration ranges from acute single doses to eight-week safety studies. Systematically missing are: (1) long-term studies over several months, (2) investigations of theacrine as a single substance at high doses, (3) studies with clinical biomarkers (e.g., inflammation, metabolism) and (4) population-specific data (e.g., older adults, patients with metabolic diseases).]

Theacrine: A caffeine substitute or an independent active substance?

Theacrine is often marketed as a
'NON-HABITUATING CAFFEINE ANALOGUE'

, but the evidence base presents a more nuanced picture. While theacrine lacks **acute stimulation** and **tolerance effects** appear to be lower, the **mechanisms of action** are not identical. Whereas caffeine primarily **blocks adenosine receptors**, theacrine also modulates **dopamine and noradrenaline systems**, leading to a **delayed but longer-lasting effect**. This explains why theacrine often shows **no immediate performance enhancement** in studies, but measurable effects after **30–60 minutes**.

A central issue is the
LACK OF DIFFERENTIATION FROM CAFFEINE

. Many studies examine theacrine in **combination with caffeine**, which complicates interpretation. The **most cited study from 2017** (23 citations) shows that theacrine has **no significant interactions** with caffeine, but whether it is **equally effective alone** remains unclear. In addition, **long-term studies** are lacking to confirm whether theacrine truly **does not induce tolerance**—a frequently claimed advantage over caffeine.

3. How Robust Is the Research?

Research on theacrine spans **three main application areas**: **fatigue** (7 studies), **cognitive performance** (5 studies) and **cardiovascular parameters** (5 studies). In addition, there are individual studies on **safety**, **musculoskeletal system**, **immune system** and **gut health**. Notably, most controlled studies investigate **acute effects**—i.e., the effect after single or short-term intake. Long-term studies are still missing. The **most cited works** (2017–2021) originate from **sports science** and **cognitive psychometrics**, reflecting the current research focus.

Methodologically, the field is **heterogeneous**: while some studies are **placebo-controlled and double-blind**, others lack **long-term data** or **large sample sizes**. The **safety studies** (5 controlled trials) show no serious adverse effects, but the **interaction with caffeine** remains controversial. Another weakness is the **lack of standardisation** in measurement methods—particularly in cognitive tests. The **most recent studies** (2024–2026) suggest that theacrine may act **synergistically in combination with other alkaloids** (e.g., methylxanthines), complicating the interpretation of results.

4. What Is Often Claimed — and What the Data Show

STATEMENT	STUDY EVIDENCE
Theacrine as a performance booster in sport	The studies show no consistent increase in physical performance. Individual studies suggest improved endurance , but the effects are small and not reproducible .
Theacrine as a nootropic	Cognitive tests showed slightly improved reaction times and attention , but no significant enhancement in memory performance . The effects were weaker than caffeine .
Theacrine as a safe alternative to caffeine	Safety studies show no serious adverse effects , but long-term tolerability has not been investigated. Interactions with other stimulants are possible.
Theacrine for chronic fatigue	The studies examine acute effects in healthy volunteers. Whether theacrine is effective in chronic fatigue or fatigue syndromes remains unresolved .

5. Profile: Molecule and Charge

Theacrine is not a single molecule but a **mixture** — there is no molecular formula or fixed molecular mass. What can be described are functional groups, charge behaviour and redox properties; this is the focus of the next section.

6. Interactions with Other Substances

With which other substances on this platform this compound has been **jointly** studied or discussed in human trials and reviews — combinations, comparisons or shared mechanisms. The number refers to studies in which both were investigated.

SUBSTANCE	JOINT STUDIES	CONTROLLED IN HUMANS
Stress, cortisol and inflammation	4	4
Chronic inflammation	2	0

Pharmacokinetic interaction with caffeine: Theacrine shows a clinically relevant interaction with caffeine that increases exposure to theacrine. When co-administered, the maximum plasma concentration (C_{max}) and the area under the concentration-time curve (AUC) of theacrine increased without altering its half-life^{3,3}. Despite this pharmacokinetic change, haemodynamic parameters such as heart rate and blood pressure remained unchanged, suggesting safe co-use at the tested doses³. A genetic variation in the *CYP1A2* enzyme (*CYP1A2*1F allele status) had no moderating effect on study outcomes^{4,4}.

Combination effects with other stimulants: Theacrine acts structurally and functionally similar to caffeine as an adenosine receptor antagonist. Additionally, the tolerability of theacrine in combination with methylxanthines (Dynamine®) was examined over four weeks, with no adverse effects on health markers observed^{10,10}. Whether theacrine interacts with other drugs or nutrients metabolised via *CYP* enzymes remains to be clarified.

7. Overdose, Tolerability, Limits

Proven: Adverse effects and safety markers in humans In controlled studies and observations lasting up to eight weeks, theacrine showed no changes in resting heart rate, blood pressure, gas exchange or systemic haemodynamics¹. Clinical safety markers (lipid profiles, blood count, liver/kidney/immune function values) remained within normal ranges without group or time interactions at daily doses of up to 300 mg¹¹. However, at doses of 3 or 6 mg/kg body weight, adverse effects such as gastrointestinal complaints, perceived tachycardia, dizziness, headache, hand tremor and lassitude were reported¹². In a study with 20 participants (age 21.5 ± 3.8 years), no habituation effects were observed, though the reported side effects may limit suitability as a supplement^{11,12}.

Plausible: Dosage and contraindications The longest documented human use duration is eight weeks with a maximum daily dose of 300 mg, without evidence of tolerance development¹¹. Compared to caffeine, theacrine is attributed a longer half-life and lower habituation, though long-term data are lacking^{7,6}. As theacrine structurally resembles caffeine, individuals with caffeine hypersensitivity (e.g., sleep disturbances, restlessness) may experience similar reactions. It remains unclear whether pre-existing cardiovascular conditions or interactions with other stimulants increase the risk of observed adverse effects. Further investigation is needed to determine whether lower doses (below 3 mg/kg) improve tolerability and whether individual factors (e.g., genetics, metabolism) influence the response.

8. The Most Robust Studies

Ordered by evidence strength, not by prominence. The full evaluation includes significantly more studies; here, the most reliable are listed.

Controlled Human Studies

- ¹ A Two-Part Approach to Examine the Effects of Theacrine (TeaCrine®) Supplementation on Oxygen Consumption, Hemodynamic Responses, and Subjective Measures (2017)
- ² The effects of a caffeine-like supplement, TeaCrine®, on muscular strength, endurance and power performance in resistance-trained men (2019)
- ³ Assessment of the Drug-Drug Interaction Potential Between Theacrine and Caffeine in Humans (2017)
- ⁴ A Combination of Caffeine, TeaCrine® (Theacrine), and Dynamine® (Methylxanthine) Increases Cognitive Performance and Reaction Time Without Interfering (2021)
- ⁵ Effects of caffeine, methylxanthine, and theacrine on vigilance, marksmanship, and hemodynamic responses in tactical personnel: a double-blind, random (2022)
- ⁶ Theacrine as a novel ergogenic aid: impact on canoe sprint performance (2025)
- ⁷ A caffeine and theacrine combination improves cognitive performance in tactical personnel under physically fatiguing conditions (2025)
- ⁸ Assessing the impact of high theacrine doses on hemodynamic measures, cognitive performance, and physiological stress (2026)
- The Effect of Short-Term NAD3® Supplementation on Circulating Adult Stem Cells in Healthy Individuals Aged 40-70 Years (2024)

Observational Human Studies

- Safety of TeaCrine®, a non-habituating, naturally-occurring purine alkaloid over eight weeks of continuous use (2016)
- ⁹ Cognitive Performance and Mood Following Ingestion of a Theacrine-Containing Dietary Supplement, Caffeine, or Placebo by Young Men and Women (2015)

9. Summary

Evidence: In controlled human studies, theacrine consistently improves subjective parameters such as energy, focus, and motivation, particularly when combined with caffeine or methylxanthine. Cognitive enhancements (reaction time, inhibitory control) have been demonstrated in esports and tactical populations, while haemodynamic parameters remain stable—even at high doses. Safety studies over up to eight weeks report no serious adverse effects, though long-term data are lacking. The bioavailability of theacrine is increased by caffeine without affecting its metabolism. Its delayed and prolonged action distinguishes theacrine from caffeine, making it suitable for sustained-demand applications.

PLAUSIBLE Preclinical and early human studies suggest additional mechanisms beyond adenosinergic modulation. **Hypothesis:** The inhibition of proinflammatory pathways (e.g., NF-κB) observed in animal studies may be relevant for chronic inflammatory processes. Structural similarities to caffeine also suggest potential effects on purine metabolism or mitochondrial function, which could explain metabolic outcomes. The observed increase in vascular repair cells (CD45dimCD34+CD309+) in a theacrine-containing supplement study may indicate potential for tissue regeneration. **Hypothesis:** Elevated cortisol levels in a high-dose study could reflect an adaptogenic effect protective under chronic stress, though systematic investigations are lacking.

What remains to be clarified: Research on theacrine is still in its early stages, particularly regarding its evaluation as a standalone substance. A study should investigate high doses (e.g., 300–400 mg) over several months in healthy adults to assess long-term effects on cognition, cardiovascular parameters, and tolerance development. Additionally, clinical biomarkers such as inflammatory markers (CRP, cytokines), metabolic parameters (glucose tolerance, lipid profile), and stem cell populations should be systematically recorded to validate preclinical findings. A population-specific study involving older adults or patients with chronic stress could determine whether adaptogenic or anti-inflammatory effects are clinically relevant. Finally, a direct comparative study of theacrine and caffeine at equivalent doses would be necessary to verify claimed advantages (no tolerance development, more favourable side-effect profile).

10. Open Questions

- **Dosage:** What is the optimal amount of theacrine for cognitive or physical effects?
- **Long-term effects:** Does theacrine lead to tolerance or habituation like caffeine?
- **Combination therapies:** Does theacrine act synergistically with other alkaloids or nootropics?

11. Further Paths

Topics, mechanisms, and pathways in which this substance is involved — for those looking beyond the substance itself.

- Interaction network

Topics, mechanisms and chains in which this substance appears — for those who want to look beyond the substance.

Frequently Asked Questions

Can theacrine replace caffeine?

Proven: Theacrine shows **no acute stimulation** like caffeine, but a **delayed and prolonged effect**. Studies suggest **no tolerance development**, yet whether it can **fully replace caffeine** remains unclear. Most trials examine theacrine **in combination with caffeine**, complicating interpretation. **Long-term studies** and **head-to-head comparisons** are needed for a definitive assessment.

Are there side effects of theacrine?

Proven: Controlled trials report **no serious adverse events** with short-term use. Possible effects include **mildly increased heart rate** or **restlessness**, similar to caffeine but **less pronounced**. **Long-term safety** has not been evaluated. Interactions with other **stimulants** or **medications** are plausible but not systematically studied.

How quickly does theacrine take effect?

Proven: Unlike caffeine, theacrine shows **no immediate onset**. Measurable effects appear after **30–60 minutes** and may persist for **up to 6 hours**. This reflects **delayed absorption** and a **distinct mechanism** involving adenosine receptors and neurotransmitter modulation.

Sources

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- 3 Assessment of the Drug-Drug Interaction Potential Between Theacrine and Caffeine in Humans
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- 6 Theacrine as a novel ergogenic aid: impact on canoe sprint performance
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- 7 A caffeine and theacrine combination improves cognitive performance in tactical personnel under physically fatiguing conditions
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- 9 Cognitive Performance and Mood Following Ingestion of a Theacrine-Containing Dietary Supplement, Caffeine, or Placebo by Young Men and Women
Kuhman DJ, Joyner KJ, Bloomer RJ · 2015
- 10 Safety of Short-Term Supplementation with Methylxanthine (Dynamine®) Alone and in Combination with TeaCrine...
· 2020
- 11 No evidence of habituation was noted as baseline values for energy, focus, concentration, anxiety, motivation to exercise...
· 2016
- 12 Some side effects, such as gastrointestinal discomfort, perception of tachycardia, dizziness, headache, head pressure, h...
· 2025
- 13 Theacrine From Camellia kucha and Its Health Beneficial Effects
Sheng YY, Xiang J, Wang ZS, Jin J, Wang YQ, Li QS et al. · 2020
- 14 Systematic Identification of Characteristic Metabolites and Analysis of Quality and Metabolomic Profiles of Yunnan Kucha White Tea
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International Health Research

Research, put in context. Every statement leads to the original paper; the decision in the individual case rests with the treating professional.
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