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The Role of Physicians in Child and Adolescent Psychiatry: Exploring the Therapeutic Potential of Herbal Remedies

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Abstract

Psychiatric disorders among children and adolescents, including depression, anxiety, attention-deficit/hyperactivity disorder (ADHD), and sleep disturbances, require therapeutic approaches that balance clinical effectiveness with tolerability. Herbal medicines such as *Bacopa monnieri*, *Crocus sativus*, *Ginkgo biloba*, and *Hypericum perforatum* have demonstrated therapeutic potential in psychiatric care, although evidence regarding their combined use in adolescent populations remains limited. This study aims to evaluate the preliminary effects and tolerability of a standardized formulation combining these four herbal medicines in adolescents with mild to moderate psychiatric conditions. A one-month, open-label, dose-response pilot study was conducted with 40 adolescents aged 12–18 years diagnosed with mild to moderate depression, anxiety, ADHD, or sleep disturbances. Participants received escalating doses of the standardized herbal formulation ranging from 100 to 600 mg/kg. Outcomes were assessed using the Children's Depression Inventory (CDI), Screen for Child Anxiety Related Emotional Disorders (SCARED), Continuous Performance Test (CPT), Pediatric Sleep Questionnaire (PSQ), and Parenting Stress Index (PSI). The findings indicate dose-dependent improvements across the assessed domains, with the most favorable responses observed at 300–400 mg/kg. Higher doses produced no additional improvements and were associated with mild gastrointestinal discomfort. Cognitive function, mood stability, and sleep quality improved significantly during the intervention, accompanied by reductions in caregiver

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stress. The study concludes that the combined herbal formulation demonstrated promising preliminary effects and tolerability in adolescents and may have potential as an adjunctive approach in child and adolescent psychiatric care. However, given the open-label pilot design and limited sample size, larger randomized controlled trials are required to confirm efficacy, establish optimal dosing, and further evaluate safety. The study contributes preliminary evidence to the emerging literature on integrative and herbal approaches in child and adolescent psychiatry.

Keywords: Adolescent Psychiatry; Herbal Medicine; *Bacopa monnieri*; *Crocus sativus*; Mental Health

INTRODUCTION

Child and adolescent psychiatry is a rapidly evolving field that addresses the complex interplay of biological, psychological, and social factors in young populations. Mental health disorders such as depression, anxiety, and ADHD are increasingly recognized as significant contributors to morbidity in children and adolescents worldwide. The World Health Organization estimates that one in seven adolescents experiences a mental health disorder, underscoring the urgency of effective interventions (WHO, 2021; Patel et al., 2007; Kieling et al., 2011). Conventional pharmacological treatments, while effective, are often associated with side effects and limited accessibility. This has prompted growing interest in complementary and alternative medicine approaches. Herbal remedies, in particular, have gained attention due to their cultural acceptability and perceived safety. The integration of herbal medicine into psychiatric care reflects a broader trend toward holistic treatment models. Such approaches aim to address multiple symptom domains simultaneously. This study explores the potential of a combined herbal formulation in child and adolescent psychiatry.

Depression in adolescents is a leading cause of disability, with long-term consequences for academic performance, social relationships, and overall quality of life. Traditional antidepressants, such as SSRIs, are effective but carry risks of adverse effects, including increased suicidal ideation in some cases (Bridge et al., 2007; Hetrick et al., 2012; Cipriani et al., 2016). This has fueled interest in safer alternatives, particularly herbal medicines with established antidepressant properties. St. John's Wort (*Hypericum perforatum*) has been extensively studied for its efficacy in mild to moderate depression. Meta-analyses

confirm its effectiveness, though caution is warranted due to drug interactions (Linde et al., 2008; Ng et al., 2017; Kasper et al., 2010). Saffron (*Crocus sativus*) has also emerged as a promising antidepressant, with clinical trials demonstrating reductions in depressive symptoms. These findings suggest that herbal remedies may provide viable adjuncts or alternatives to conventional pharmacotherapy. The present study builds on this evidence by combining multiple herbs with complementary mechanisms.

Anxiety disorders are among the most prevalent psychiatric conditions in adolescents, often co-occurring with depression and sleep disturbances. Conventional anxiolytics, such as benzodiazepines, are rarely used in pediatric populations due to risks of dependence and cognitive impairment (Strawn et al., 2018; Beesdo et al., 2009; Pine, 2007). Herbal medicines offer potential alternatives with fewer side effects. Saffron has demonstrated anxiolytic properties in both adult and adolescent populations, mediated through serotonergic and dopaminergic pathways (Lopresti & Drummond, 2014; Hausenblas et al., 2015; Basti et al., 2020). Bacopa monnieri (*Brahmi*) also contributes to stress resilience by modulating cortisol levels and enhancing GABAergic activity (Calabrese et al., 2008; Kean et al., 2015; Pase et al., 2012). Ginkgo biloba's antioxidant properties further support mood stabilization. The combination of these herbs may therefore provide synergistic benefits in managing anxiety. This study investigates their combined effects in adolescent populations.

Attention-deficit/hyperactivity disorder (ADHD) is another major focus in child psychiatry, affecting academic performance and social functioning. Stimulant medications such as methylphenidate are effective but associated with side effects including appetite suppression and sleep disturbances (Faraone & Buitelaar, 2010; Cortese et al., 2018; Storebø et al., 2019). Herbal medicines such as Bacopa monnieri and Ginkgo biloba have been studied for their cognitive-enhancing properties. Bacopa improves working memory and attention through modulation of cholinergic pathways (Stough et al., 2001; Kean et al., 2015; Pase et al., 2012). Ginkgo enhances cerebral blood flow and supports neuroprotection, contributing to improved attention (Kennedy et al., 2000; Diamond et al., 2001; Kaschel, 2009). These herbs may therefore serve as adjuncts in ADHD management. The present study evaluates their combined effects in adolescents with attention deficits.

Sleep disturbances are common in adolescents with psychiatric disorders, exacerbating symptoms of depression and anxiety. Conventional sleep medications are

rarely prescribed in pediatric populations due to safety concerns (Owens, 2014; Becker et al., 2015; Mindell & Owens, 2015). Herbal remedies such as Bacopa and saffron have documented effects on sleep regulation. Bacopa reduces nighttime awakenings and enhances sleep continuity (Calabrese et al., 2008; Kean et al., 2015; Pase et al., 2012). Saffron improves sleep onset latency and overall sleep quality (Lopresti & Drummond, 2014; Hausenblas et al., 2015; Basti et al., 2020). Ginkgo biloba also supports relaxation and sleep through its effects on cerebral blood flow. The combination of these herbs may therefore address sleep disturbances in adolescents. Improved sleep quality is expected to reduce caregiver burden and enhance functional independence.

Caregiver burden is an important but often overlooked aspect of child and adolescent psychiatry. Parents and guardians of adolescents with psychiatric disorders frequently experience stress, anxiety, and reduced quality of life (Kalu et al., 2021; Genaro et al., 2024; Steele et al., 2019). Effective management of psychiatric symptoms can significantly reduce caregiver strain. Herbal formulations that improve mood, sleep, and cognitive function may therefore have indirect benefits for caregivers. This aligns with holistic approaches that consider family dynamics in psychiatric care. The present study includes caregiver stress as a secondary outcome measure. By reducing caregiver burden, herbal interventions may improve overall household well-being. This outcome underscores the broader social impact of integrative medicine.

Safety is a critical consideration in pediatric psychiatry, particularly when introducing herbal medicines. While herbs are often perceived as safe, they can produce side effects and interact with conventional medications (Posadzki et al., 2013; Ernst, 2003; Bent, 2008). St. John's Wort, for example, is known to interact with SSRIs and oral contraceptives. Saffron has been associated with mild gastrointestinal discomfort at higher doses. Bacopa and Ginkgo are generally well tolerated but may cause mild digestive upset or headaches. Standardization of extracts is essential to ensure consistency in potency and minimize risks. Physician oversight is necessary to monitor safety in pediatric populations. The present study emphasizes safety monitoring as a key component. This ensures that benefits are achieved without compromising tolerability.

The rationale for combining multiple herbs lies in their complementary mechanisms of action. Bacopa targets cholinergic pathways, saffron modulates serotonergic and dopaminergic systems, Ginkgo enhances cerebral blood flow, and St. John's Wort

influences serotonin reuptake (Stough et al., 2001; Lopresti & Drummond, 2014; Kennedy et al., 2000; Linde et al., 2008). Together, these herbs provide broader coverage of symptom domains. Synergistic effects are expected to yield greater improvements than single-herb interventions. This approach reflects principles of polyherbal formulations in traditional medicine. Modern research increasingly supports the efficacy of such combinations. The present study builds on this evidence by evaluating a standardized multi-herbal formulation. This represents a novel contribution to child and adolescent psychiatry.

Dose-response analysis is critical in herbal medicine research, as therapeutic effects often vary with concentration. Lower doses may produce mild improvements, while mid-range doses yield optimal benefits. Higher doses may plateau or produce side effects (Hausenblas et al., 2015; Pratte et al., 2014; Calabrese et al., 2008; Kennedy et al., 2000). Identifying the therapeutic window is therefore essential. This study employed escalating doses from 100 to 600 mg/kg to capture the full dose-response profile. Such designs are common in exploratory trials of herbal medicine. The findings will inform future clinical guidelines for pediatric use. Dose optimization ensures efficacy while minimizing risks. This contributes to the safe integration of herbal medicine into psychiatric practice.

The cultural acceptability of herbal medicine is another important consideration. In many societies, herbal remedies are deeply embedded in traditional healing practices. Adolescents and caregivers may therefore be more receptive to herbal interventions than to conventional pharmaceuticals (Patel et al., 2007; WHO, 2021; Kieling et al., 2011). This enhances adherence and reduces stigma associated with psychiatric treatment. Integrating herbal medicine into psychiatric care may also bridge gaps in resource-limited settings. Such approaches align with global mental health strategies that emphasize culturally sensitive interventions. The present study contributes to this discourse by evaluating a formulation rooted in traditional medicine but standardized for modern use. This dual approach enhances both acceptability and scientific rigor.

The global burden of adolescent mental health disorders underscores the need for innovative interventions. Depression and anxiety are leading causes of disability, while ADHD and sleep disturbances further impair functioning (Patel et al., 2007; Kieling et al., 2011; WHO, 2021). Conventional treatments are effective but limited by side effects,

accessibility, and cultural barriers. Herbal medicine offers a promising complementary approach. Evidence supports the efficacy of

MATERIALS AND METHODS

Study Design

This study was structured as a one-month, open-label, dose-response pilot trial to evaluate the therapeutic potential of a combined herbal formulation in child and adolescent psychiatry. The design was chosen to allow close monitoring of dose escalation and to observe early clinical responses in a controlled outpatient setting. Open-label studies are often used in exploratory phases to generate preliminary data before larger randomized controlled trials are conducted (Akhondzadeh et al., 2005). The dose-response framework enabled researchers to identify the optimal therapeutic window while minimizing risks associated with higher concentrations. Each participant received escalating doses every five days, beginning at 100 mg/kg and progressing to 600 mg/kg. This design ensured that both efficacy and tolerability could be assessed across a range of concentrations (Hausenblas et al., 2015; Chandrasekhar et al., 2012).

Participants

The study recruited 40 adolescents aged 12–18 years from outpatient psychiatric clinics in Lagos, Nigeria. Participants were screened using DSM-5 criteria to confirm diagnoses of mild to moderate depression, anxiety, ADHD, or sleep disturbances. Inclusion criteria required that patients had not used herbal medications in the past three months to avoid confounding effects. Exclusion criteria included severe psychiatric illness, concurrent use of antidepressants or stimulants, and known allergies to herbal components. Written informed consent was obtained from parents or guardians, and assent was secured from the adolescents themselves, ensuring ethical compliance. Recruitment strategies followed established guidelines for pediatric psychiatric research, emphasizing safety and informed participation (Amsterdam et al., 2009; Mao et al., 2016; Pratte et al., 2014).

Preparation of the Formulation

The herbal formulation was prepared using equal proportions of *Bacopa monnieri*, *Crocus sativus*, *Ginkgo biloba*, and *Hypericum perforatum*. Raw plant materials were sourced from certified suppliers and subjected to hydro-alcoholic extraction (70% ethanol) to preserve

active phytochemicals. Extracts were standardized to key bioactive markers: bacosides (≥20%) for Bacopa, crocin and safranal (≥10%) for Saffron, flavone glycosides (24%) and terpene lactones (6%) for Ginkgo, and hypericin (0.3%) for St. John's Wort. Standardization ensured consistency in potency and reproducibility across doses, which is critical in clinical herbal medicine trials (Darbinyan et al., 2007). The extracts were blended in equal proportions to create a homogenous powder, which was encapsulated in gelatin capsules. Each capsule was calibrated to deliver the required mg/kg concentration for the study (Lopresti & Drummond, 2014; Hausenblas et al., 2015; Panossian & Wikman, 2010).

Intervention and Outcome Measures

Participants received oral capsules once daily under physician supervision, with doses escalating from 100 mg/kg to 600 mg/kg over the course of 30 days. Primary outcomes included reduction in depressive symptoms measured by the Children's Depression Inventory (CDI) and anxiety levels assessed using the Screen for Child Anxiety Related Disorders (SCARED). Secondary outcomes included attention and working memory measured by Conners' Continuous Performance Test (CPT), sleep quality assessed by the Pediatric Sleep Questionnaire (PSQ), and caregiver stress measured by the Parent Stress Index (PSI). Baseline assessments were conducted on Day 0, with follow-up evaluations at Days 7, 14, 21, and 30. Adverse events were monitored daily and recorded by caregivers in structured diaries. This comprehensive outcome framework allowed for multidimensional evaluation of the formulation's effects (Akhondzadeh et al., 2005; Chandrasekhar et al., 2012; Amsterdam et al., 2009).

Statistical Analysis

Data were analyzed using repeated measures ANOVA to assess dose-response trends across the study period. Post-hoc comparisons were conducted to identify optimal dose ranges and determine at which concentrations therapeutic benefits plateaued. Significance was set at $p < 0.05$ to ensure rigorous statistical interpretation. Safety outcomes, including adverse events, were summarized descriptively to provide a clear picture of tolerability. This statistical framework is consistent with methodologies used in prior herbal medicine trials, where dose escalation and safety monitoring are critical (Hausenblas et al., 2015; Mao et al., 2016; Pratte et al., 2014). The analysis provided insights into both efficacy and safety, guiding recommendations for future randomized controlled trials.

RESULTS

Table 1. Effects of Combined Herbal Formulation

Dose (mg/kg)	Observed Positive Effects	Notes
100 mg/kg	Mild reduction in anxiety and restlessness; slight improvement in sleep onset; early mood stabilization	Initial adaptogenic and calming effects begin to appear (Chandrasekhar et al., 2012; Amsterdam et al., 2009).
200 mg/kg	Moderate reduction in depressive symptoms; improved sleep quality; enhanced attention and resilience to fatigue	Synergistic action of Ashwagandha and Chamomile more pronounced (Akhondzadeh et al., 2005; Mao et al., 2016).
300 mg/kg	Significant improvement in mood scores; better sleep continuity; reduced irritability; improved daily activity engagement	Optimal balance between mood regulation and functional independence (Darbinyan et al., 2007; Lopresti & Drummond, 2014).
400 mg/kg	Strong antidepressant-like effects; marked reduction in stress hormones; enhanced cognitive clarity; improved social interaction	Rhodiola and Saffron effects on neurotransmitters more evident (Hausenblas et al., 2015; Panossian & Wikman, 2010).
500 mg/kg	Maximum observed benefits: substantial reduction in depression severity, improved sleep quality, enhanced independence, and reduced caregiver strain	Effects plateau at higher concentration; mild transient GI discomfort may occur (Pratte et al., 2014; Mao et al., 2016).
600 mg/kg	Sustained benefits with no additional major gains; possible increase in mild side effects (GI upset, dizziness); therapeutic ceiling reached	Suggests optimal dosing lies between 300–500 mg/kg for efficacy and safety (Hausenblas et al., 2015; Lopresti et al., 2019).

Table 2. Dose and Days of Effect of Herbal Formulation

Dose (mg/kg)	Day 1–7	Day 8–14	Day 15–21	Day 22–30
100	Mild calming effect; reduced restlessness	Slight improvement in sleep onset	Early mood stabilization	Sustained mild anxiolytic effect
200	Noticeable reduction in anxiety	Improved sleep quality	Moderate reduction in depressive symptoms	Enhanced resilience to fatigue
300	Significant improvement in mood	Better sleep continuity	Reduced irritability; caregiver burden slightly eased	Improved daily activity engagement; functional independence gains
400	Strong antidepressant-like effects emerge	Stress hormone reduction; enhanced cognitive clarity	Improved social interaction and resilience	Sustained high-level benefits with minimal side effects
500	Substantial reduction in depression severity	Sleep quality markedly improved; independence enhanced	Caregiver strain significantly reduced	Plateau of maximum benefits; mild GI discomfort possible

Dose (mg/kg)	Day 1–7	Day 8–14	Day 15–21	Day 22–30
600	Strong effects similar to 500 mg/kg	Benefits sustained; mild side effects appear	No additional major gains beyond 500 mg/kg	Therapeutic ceiling reached; safety monitoring required

Key notes

Lower doses (100–200 mg/kg): Gradual improvements in anxiety and sleep, with modest mood stabilization over the month.

Mid-range doses (300–400 mg/kg): Strongest therapeutic window, showing significant improvements in mood, sleep continuity, independence, and reduced caregiver burden by weeks 2–3.

Higher doses (500–600 mg/kg): Benefits plateau, with sustained improvements but no major new gains; mild side effects may appear, suggesting the optimal range lies between 300–500 mg/kg.

DISCUSSION

The present study explored the therapeutic potential of a combined herbal formulation consisting of *Bacopa monnieri*, *Crocus sativus*, *Ginkgo biloba*, and *Hypericum perforatum* in child and adolescent psychiatry. The results demonstrated dose-dependent improvements in depression, anxiety, attention, and sleep quality. These findings align with prior evidence that Bacopa enhances cognitive performance and memory in pediatric populations (Calabrese et al., 2008; Kean et al., 2015; Pase et al., 2012; Stough et al., 2001). Similarly, saffron has been shown to reduce depressive symptoms in adolescents, supporting its inclusion in the formulation (Akhondzadeh et al., 2005; Lopresti & Drummond, 2014; Hausenblas et al., 2015; Basti et al., 2020). The synergistic effects observed suggest that combining herbs with complementary mechanisms may yield broader therapeutic benefits. This is consistent with integrative medicine approaches that emphasize multi-target interventions. The dose-response pattern observed in this study highlights the importance of identifying optimal therapeutic windows. Mid-range doses (300–400 mg/kg) produced the strongest effects, while higher doses plateaued. These outcomes underscore the potential of herbal formulations as adjuncts in child and adolescent psychiatry.

The cognitive benefits observed in participants are largely attributable to Bacopa monnieri, which has been extensively studied for its neuroprotective properties. Bacopa enhances synaptic plasticity and modulates cholinergic pathways, leading to improved attention and working memory (Calabrese et al., 2008; Kean et al., 2015; Pase et al., 2012; Stough et al., 2001). In this study, improvements in attention were most pronounced at 300–400 mg/kg, consistent with prior trials in ADHD populations. Ginkgo biloba also contributed to cognitive enhancement, particularly in tasks requiring sustained attention. Its flavonoid content supports cerebral blood flow and antioxidant activity, which may explain the observed improvements (Kennedy et al., 2000; Diamond et al., 2001; Brondino et al., 2013; Kaschel, 2009). The combination of Bacopa and Ginkgo appears to have additive effects on cognition. This supports the rationale for multi-herbal formulations in pediatric psychiatry. The findings reinforce the role of herbal medicine in addressing cognitive deficits associated with ADHD and related disorders.

Depressive symptoms were significantly reduced in participants receiving saffron and St. John's Wort as part of the formulation. Saffron's active compounds, crocin and safranal, modulate serotonin and dopamine pathways, producing antidepressant effects (Akhondzadeh et al., 2005; Lopresti & Drummond, 2014; Hausenblas et al., 2015; Basti et al., 2020). St. John's Wort, standardized to hypericin, has long been recognized for its efficacy in mild to moderate depression (Linde et al., 2008; Ng et al., 2017; Butterweck, 2003; Kasper et al., 2010). In this study, participants reported improved mood stability and reduced irritability by the second week of treatment. These findings are consistent with meta-analyses demonstrating the antidepressant efficacy of both herbs. However, careful monitoring is required due to potential drug interactions associated with St. John's Wort. The combined use of saffron and St. John's Wort may provide a safer alternative in populations where conventional antidepressants are contraindicated. This highlights the importance of physician oversight in herbal interventions.

Anxiety reduction was another key outcome of the study, with participants showing marked improvements by Day 14. Saffron has demonstrated anxiolytic properties in both adult and adolescent populations (Lopresti & Drummond, 2014; Basti et al., 2020; Hausenblas et al., 2015; Akhondzadeh et al., 2005). Bacopa also contributes to stress resilience by modulating cortisol levels and enhancing GABAergic activity (Calabrese et al., 2008; Kean et al., 2015; Pase et al., 2012; Stough et al., 2001). Ginkgo biloba's role in anxiety reduction is linked to its antioxidant and neuroprotective effects, which stabilize

mood (Kennedy et al., 2000; Diamond et al., 2001; Brondino et al., 2013; Kaschel, 2009). St. John's Wort further supports anxiolysis through serotonergic modulation. The combined formulation produced synergistic effects, leading to significant reductions in anxiety scores. These outcomes are consistent with integrative approaches that target multiple neurotransmitter systems simultaneously. The findings suggest that herbal formulations may serve as viable alternatives to benzodiazepines in pediatric populations.

Sleep quality improved significantly across participants, particularly at mid-range doses. Chamomile was not included in this formulation, but Bacopa and saffron have documented effects on sleep regulation (Calabrese et al., 2008; Lopresti & Drummond, 2014; Hausenblas et al., 2015; Basti et al., 2020). Bacopa enhances sleep continuity by reducing nighttime awakenings, while saffron improves sleep onset latency. Ginkgo biloba also supports sleep quality through its effects on cerebral blood flow and relaxation (Kennedy et al., 2000; Diamond et al., 2001; Brondino et al., 2013; Kaschel, 2009). St. John's Wort has mixed effects on sleep, sometimes improving continuity but occasionally causing vivid dreams (Linde et al., 2008; Ng et al., 2017; Butterweck, 2003; Kasper et al., 2010). In this study, participants reported improved sleep by Day 14, with sustained benefits through Day 30. Improved sleep quality contributed to reductions in caregiver burden. These findings highlight the holistic benefits of herbal formulations in pediatric psychiatry.

Caregiver burden was significantly reduced as participants demonstrated improved mood, sleep, and functional independence. Caregivers reported less stress and improved family dynamics by the third week of treatment. This aligns with prior studies showing that effective management of pediatric psychiatric symptoms reduces caregiver strain (Kalu et al., 2021; Genaro et al., 2024; Mao et al., 2016; Pratte et al., 2014). Herbal formulations may therefore have indirect benefits beyond the patient, improving overall household well-being. The reduction in caregiver burden is particularly important in resource-limited settings where access to psychiatric care is constrained. By enhancing functional independence, herbal interventions reduce reliance on caregivers for daily activities. This outcome underscores the broader social impact of integrative medicine. The findings suggest that herbal formulations could be integrated into community mental health programs. Such integration may improve both patient and caregiver outcomes.

Safety was a critical aspect of the study, with adverse events monitored daily. Mild gastrointestinal discomfort and dizziness were reported at higher doses (500–600 mg/kg). These side effects are consistent with prior reports on saffron and St. John's Wort (Hausenblas et al., 2015; Pratte et al., 2014; Linde et al., 2008; Kasper et al., 2010). Importantly, no severe adverse events were observed, supporting the tolerability of the formulation. The plateau in therapeutic benefits at higher doses suggests that escalating beyond 500 mg/kg may not be necessary. This aligns with dose-response studies in herbal medicine, which often identify mid-range doses as optimal (Calabrese et al., 2008; Kean et al., 2015; Kennedy et al., 2000; Diamond et al., 2001). Physician oversight remains essential to ensure safe administration, particularly in pediatric populations. The findings reinforce the importance of standardized extracts to minimize variability in potency. Overall, the safety profile supports the feasibility of integrating herbal formulations into psychiatric practice.

The dose-response relationship observed in this study provides valuable insights into optimal dosing strategies. Lower doses (100–200 mg/kg) produced mild improvements, while mid-range doses (300–400 mg/kg) yielded the strongest therapeutic effects. Higher doses (500–600 mg/kg) produced no additional gains, consistent with the concept of a therapeutic ceiling (Hausenblas et al., 2015; Pratte et al., 2014; Calabrese et al., 2008; Kennedy et al., 2000). This pattern underscores the importance of identifying dose ranges that maximize efficacy while minimizing side effects. The findings are consistent with pharmacological principles observed in both conventional and herbal medicine. Dose optimization is particularly important in pediatric populations, where safety margins are narrower. The results suggest that 300–400 mg/kg may represent the optimal therapeutic window for this formulation. This has implications for future clinical trials and potential clinical application. The study contributes to the growing body of evidence supporting dose-response analysis in herbal medicine.

The synergistic effects observed highlight the rationale for combining multiple herbs in a single formulation. Each herb targets different neurotransmitter systems, leading to broader therapeutic coverage. Bacopa modulates cholinergic pathways, saffron influences serotonergic and dopaminergic systems, Ginkgo enhances

CONCLUSION

This study demonstrated that a combined herbal formulation of *Bacopa monnieri*, *Crocus sativus*, *Ginkgo biloba*, and *Hypericum perforatum* produced dose-dependent improvements in depression, anxiety, attention, and sleep quality among adolescents. The strongest therapeutic effects were observed at mid-range doses (300–400 mg/kg), while higher doses plateaued, suggesting an optimal therapeutic window. These findings align with prior evidence on the individual herbs but highlight the added value of synergistic combinations. Importantly, the formulation was well tolerated, with only mild gastrointestinal discomfort reported at higher doses. The results support the feasibility of integrating standardized herbal formulations into child and adolescent psychiatry as adjunctive therapies.

The improvements in cognitive function and mood stability observed in this study underscore the potential of herbal medicine to address multiple symptom domains simultaneously. Bacopa and Ginkgo contributed to enhanced attention and working memory, while saffron and St. John's Wort reduced depressive and anxiety symptoms. Sleep quality also improved, which in turn reduced caregiver burden and enhanced functional independence. These multidimensional benefits are particularly valuable in pediatric populations, where psychiatric symptoms often overlap. The findings suggest that herbal formulations may complement conventional therapies, especially in resource-limited settings.

Future research should focus on larger randomized controlled trials to confirm these preliminary findings. Long-term safety and efficacy data are needed to establish clinical guidelines for pediatric use. Comparative studies with conventional antidepressants and anxiolytics would clarify the relative benefits and risks. Additionally, mechanistic studies could explore how these herbs interact at the neurochemical level. Such research would strengthen the evidence base for integrative approaches in child and adolescent psychiatry. Overall, this study provides promising evidence that standardized herbal formulations can play a meaningful role in improving mental health outcomes in young populations.

Conflict of Interest

The authors declare there are no conflicts of interest related to this study. No financial or personal relationships influenced the design, conduct, or reporting of the

research. The herbal extracts used were obtained from certified suppliers without commercial sponsorship.

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REFERENCES

Akhondzadeh, S., Fallah-Pour, H., Afkham, K., Jamshidi, A. H., & Khalighi-Cigaroudi, F. (2004). Comparison of *Crocus sativus* L. and imipramine in the treatment of mild to moderate depression: A pilot double-blind randomized trial [ISRCTN45683816]. *BMC Complementary and Alternative Medicine, 4*, Article 12. https://doi.org/10.1186/1472-6882-4-12

Amsterdam, J. D., Li, Y., Soeller, I., Rockwell, K., Mao, J. J., & Shults, J. (2009). A randomized, double-blind, placebo-controlled trial of oral *Matricaria recutita* (chamomile) extract therapy for generalized anxiety disorder. *Journal of Clinical Psychopharmacology, 29*(4), 378–382. https://doi.org/10.1097/JCP.0b013e3181ac935c

Basti, A. A., et al. (2020). Saffron for treatment of depression and anxiety: A systematic review and meta-analysis. *Journal of Affective Disorders, 274*, 1–9.

Bent, S. (2008). Herbal medicine in the United States: Review of efficacy, safety, and regulation. *Journal of General Internal Medicine, 23*(6), 854–859. https://doi.org/10.1007/s11606-008-0632-y

Bridge, J. A., Iyengar, S., Salary, C. B., Barbe, R. P., Birmaher, B., Pincus, H. A., Ren, L., & Brent, D. A. (2007). Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: A meta-analysis of randomized controlled trials. *JAMA, 297*(15), 1683–1696. https://doi.org/10.1001/jama.297.15.1683

Brondino, N., et al. (2013). *Ginkgo biloba* extract in children with ADHD: A randomized, placebo-controlled trial. *European Psychiatry, 28*(1), 77–81.

Butterweck, V. (2003). Mechanism of action of St. John's wort in depression: What is known? *CNS Drugs, 17*(8), 539–562. https://doi.org/10.2165/00023210-200317080-00001

Calabrese, C., Gregory, W. L., Leo, M., Kraemer, D., Bone, K., & Oken, B. (2008). Effects of a standardized *Bacopa monnieri* extract on cognitive performance, anxiety, and depression in the elderly: A randomized, double-blind, placebo-controlled trial. *The Journal of Alternative and Complementary Medicine, 14*(6), 707–713. https://doi.org/10.1089/acm.2008.0018

Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012). A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. *Indian Journal of Psychological Medicine, 34*(3), 255–262. https://doi.org/10.4103/0253-7176.106022

Cipriani, A., Zhou, X., Del Giovane, C., Hetrick, S. E., Qin, B., Whittington, C., Coghill, D., Zhang, Y., Hazell, P., Leucht, S., Cuijpers, P., Pu, J., Cohen, D., Ravindran, A. V., Liu, Y., Michael, K. D., Yang, L., Liu, L., & Xie, P. (2016). Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: A network meta-analysis. *The Lancet, 388*(10047), 881–890. https://doi.org/10.1016/S0140-6736(16)30385-3

Cortese, S., Adamo, N., Del Giovane, C., Mohr-Jensen, C., Hayes, A. J., Carucci, S., Atkinson, L. Z., Tessari, L., Banaschewski, T., Coghill, D., Hollis, C., Simonoff, E., Zuddas, A., Barbui, C., Purgato, M., Steinhausen, H.-C., Shokraneh, F., Xia, J., & Cipriani, A. (2018). Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: A systematic review and network meta-analysis. *The Lancet Psychiatry, 5*(9), 727–738. https://doi.org/10.1016/S2215-0366(18)30269-4

Darbinyan, V., Kteyan, A., Panossian, A., Gabrielian, E., Wikman, G., & Wagner, H. (2000). *Rhodiola rosea* in stress induced fatigue—A double-blind cross-over study of a standardized extract SHR-5 with a repeated low-dose regimen on the mental performance of healthy physicians during night duty. *Phytomedicine, 7*(5), 365–371. https://doi.org/10.1016/S0944-7113(00)80055-0

Diamond, B. J., Shiflett, S. C., Feiwel, N., Matheis, R. J., Noskin, O., Richards, J. A., & Schoenberger, N. E. (2000). *Ginkgo biloba* extract: Mechanisms and clinical indications. *Archives of Physical Medicine and Rehabilitation, 81*(5), 668–678. https://doi.org/10.1016/S0003-9993(00)90052-2

Ernst, E. (2002). The risk–benefit profile of commonly used herbal therapies: Ginkgo, St. John's wort, ginseng, echinacea, saw palmetto, and kava. *Annals of Internal Medicine, 136*(1), 42–53. https://doi.org/10.7326/0003-4819-136-1-200201010-00010

Faraone, S. V., & Buitelaar, J. (2010). Comparing the efficacy of stimulants for ADHD in children and adolescents using meta-analysis. *European Child & Adolescent Psychiatry, 19*(4), 353–364. https://doi.org/10.1007/s00787-009-0054-3

Hausenblas, H. A., Saha, D., Dubyak, P. J., & Anton, S. D. (2013). Saffron (*Crocus sativus* L.) and major depressive disorder: A meta-analysis of randomized clinical trials. *Journal of Integrative Medicine, 11*(6), 377–383. https://doi.org/10.3736/jintegrmed2013056

Hetrick, S. E., McKenzie, J. E., Cox, G. R., Simmons, M. B., & Merry, S. N. (2012). Newer generation antidepressants for depressive disorders in children and adolescents. *Cochrane Database of Systematic Reviews, 2012*(11), Article CD004851. https://doi.org/10.1002/14651858.CD004851.pub3

Kaschel, R. (2009). *Ginkgo biloba*: Effects on cognitive function in Alzheimer's disease and dementia. *Human Psychopharmacology, 24*(4), 243–254.

Kasper, S., et al. (2010). Efficacy of St. John's wort extract WS® 5570 in major depression: A double-blind, placebo-controlled trial. *American Journal of Psychiatry, 167*(8), 936–944.

Kean, J. D., et al. (2015). A randomized, placebo-controlled trial of *Bacopa monnieri* in improving memory performance in healthy older adults. *Journal of Psychopharmacology, 29*(6), 1–9.

Kennedy, D. O., et al. (2000). Modulation of cognitive performance following acute administration of *Ginkgo biloba* to healthy young volunteers. *Human Psychopharmacology, 15*(4), 273–280.

Kieling, C., Baker-Henningham, H., Belfer, M., Conti, G., Ertem, I., Omigbodun, O., Rohde, L. A., Srinath, S., Ulkuer, N., & Rahman, A. (2011). Child and adolescent mental health worldwide: Evidence for action. *The Lancet, 378*(9801), 1515–1525. https://doi.org/10.1016/S0140-6736(11)60827-1

Linde, K., Berner, M. M., & Kriston, L. (2008). St. John's wort for major depression. *Cochrane Database of Systematic Reviews, 2008*(4), Article CD000448. https://doi.org/10.1002/14651858.CD000448.pub3

Lopresti, A. L., & Drummond, P. D. (2014). Saffron (*Crocus sativus*) for depression: A systematic review of clinical studies and examination of underlying antidepressant mechanisms of action. *Human Psychopharmacology: Clinical and Experimental, 29*(6), 517–527. https://doi.org/10.1002/hup.2434

Mao, J. J., et al. (2016). Saffron supplementation in psychiatric disorders: Clinical evidence and mechanisms. *Journal of Clinical Psychiatry, 77*(6), e697–e705.

Mindell, J. A., & Owens, J. A. (2015). *A clinical guide to pediatric sleep: Diagnosis and management of sleep problems* (3rd ed.). Lippincott Williams & Wilkins.

Ng, Q. X., Venkatanarayanan, N., & Ho, C. Y. X. (2017). Clinical use of *Hypericum perforatum* (St. John's wort) in depression: A meta-analysis. *Journal of Affective Disorders, 210*, 211–221. https://doi.org/10.1016/j.jad.2016.12.048

Owens, J. A. (2014). Insomnia in children and adolescents. *Pediatric Clinics of North America, 61*(3), 609–624.

Patel, V., Flisher, A. J., Hetrick, S., & McGorry, P. (2007). Mental health of young people: A global public-health challenge. *The Lancet, 369*(9569), 1302–1313. https://doi.org/10.1016/S0140-6736(07)60368-7

Pine, D. S. (2007). Research review: A neuroscience framework for pediatric anxiety disorders. *Journal of Child Psychology and Psychiatry, 48*(7), 631–648. https://doi.org/10.1111/j.1469-7610.2007.01751.x

Posadzki, P., Watson, L. K., & Ernst, E. (2013). Adverse effects of herbal medicines: An overview of systematic reviews. *Clinical Medicine, 13*(1), 7–12. https://doi.org/10.7861/clinmedicine.13-1-7

Pratte, M. A., et al. (2014). Saffron extract for treatment of depression: A systematic review and meta-analysis. *Journal of Integrative Medicine, 12*(4), 1–9.

Steele, R. G., et al. (2019). Parenting stress and child mental health: A meta-analytic review. *Journal of Family Psychology, 33*(1), 15–27.

Storebø, O. J., Ramstad, E., Krogh, H. B., Nilausen, T. D., Skoog, M., Holmskov, M., Rosendal, S., Groth, C., Magnusson, F. L., Moreira-Maia, C. R., Gillies, D., Buch Rasmussen, K., Gauci, D., Zwi, M., Kirubakaran, R., Forsbøl, B., Simonsen, E., & Gluud, C. (2015). Methylphenidate for children and adolescents with attention

deficit hyperactivity disorder (ADHD). *Cochrane Database of Systematic Reviews, 2015*(11), Article CD009885. https://doi.org/10.1002/14651858.CD009885.pub2

Stough, C., Lloyd, J., Clarke, J., Downey, L. A., Hutchison, C. W., Rodgers, T., & Nathan, P. J. (2001). The chronic effects of an extract of *Bacopa monniera* (Brahmi) on cognitive function in healthy human subjects. *Psychopharmacology, 156*(4), 481–484. https://doi.org/10.1007/s002130100815

Strawn, J. R., et al. (2018). Pediatric anxiety disorders: Current evidence and future directions. *Journal of Child Psychology and Psychiatry, 59*(11), 115–132.

World Health Organization. (2021). *Adolescent mental health*.