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Effects of ashwagandha (*Withania somnifera*) on mental health in adults: A systematic review and dose–response meta-analysis of randomized controlled trials

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ABSTRACT

Background: Ashwagandha (*Withania somnifera*), as an important herbal medicine, has been increasingly recognized for its role in mental health management, particularly in reducing stress and anxiety, and reflects the growing relevance of complementary and alternative medicine in addressing psychological well-being. The present study aims to investigate its effectiveness by pooling the evidence from existing randomized controlled trials (RCTs).

Methods: Major medical databases of PubMed, Scopus, and Web of Science Core Collection were searched. Eligible studies were included. Meta-analysis, meta-regression, non-linear dose-response analysis, and subgroup analyses were conducted. Standardized mean differences (SMDs) were calculated. P-values < 0.05 were considered as statistically significant. The study protocol was registered in the PROSPERO database (CRD420251073134).

Results: Twenty-two studies met the eligibility criteria and were included. Meta-analysis revealed that supplementation with ashwagandha significantly improves stress (SMD = −5.88; 95 % CI: −8.15 to −3.60), depression (SMD = −5.68; 95 % CI: −8.43 to −2.94), and anxiety (SMD = −6.87; 95 % CI: −8.77 to −4.97). There was significant linear (coefficient = 0.005, P = 0.031) and non-linear (P-nonlinearity = 0.005) association between dosages of administered ashwagandha and stress levels.

Conclusion: Current evidence suggests that ashwagandha supplementation holds promising potential in alleviating symptoms of stress, anxiety, and depression. However, to strengthen these findings and translate them into clinical recommendations, well-designed, high-quality trials are still needed to address existing heterogeneity and to establish the most effective dosages and intervention durations.

1. Introduction

Psychological disorders have been increasingly highlighted in recent decades.[1] Amongst them, depression, anxiety, and stress have been documented to show ever-increasing trends, in developed and developing countries.[2] Multiple factors, including SARS Covid-19 pandemic, unemployment, economic instability, loneliness epidemic, social isolation, and swift societal shifts have contributed to the problem.[3–5] In addition to first-line strategies, including individualized therapy interventions and neurotransmitter-modifying medications, the use of complementary medicine has gained handsome popularity in those inflicted with these disorders.[6,7]

Famously known as ashwagandha, with the scientific name of *Withania somnifera*, also known as winter cherries, is an herb commonly consumed in South Asian countries.[8] The root of ashwagandha (*Withania somnifera*) has been traditionally used for centuries in Indian medicinal science, particularly within Ayurveda, for managing mental disorders.[8,9] Various phytochemical compounds with bioactive functions have been detected in the plant, including multiple witanolides, alkaloids, and several flavonoids.[10] Recent investigations have suggested potential positive role of ashwagandha in enhancing cognitive and physical performance, including some studies suggesting its possible role to ameliorate stress, anxiety, and even depression.[11] These chemicals have been shown to target the neurotransmitter imbalance usually used to

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explain the pathophysiology of these disorders.[12] However, owing to the nuanced characteristics of psychological disorders and recent evidence questioning the neurotransmitter-imbalance etiological approach as the most widely accepted explanation,[13] there is urgent need to unequivocally examine such claims. Although previous meta-analyses have investigated the effects of ashwagandha (*Withania somnifera*) on mental health outcomes, these studies were limited by methodological heterogeneity, variable outcome measures, a lack of dose–response analyses, and the growing body of newly published trials that has not yet been systematically synthesized. Therefore, a more comprehensive and updated synthesis is warranted to provide clearer evidence and guide clinical recommendations.[14–16]

Therefore, the present systematic review and meta-analysis was conducted to investigated the impact of ashwagandha products on indices measuring stress, anxiety, and depression both in individuals suffering from psychological disorders and healthy participants.

2. Methods

The present systematic review and meta-analysis study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[17] The study protocol was prospectively registered in the PROSPERO database (registration number: CRD420251073134). Eligibility criteria were defined using the PICOS framework, encompassing: participants (adults aged 18 years and older), intervention (administration of ashwagandha), comparison (a control group receiving placebo), outcomes (stress, anxiety, and depression), and study design (randomized controlled trials).

2.1. Search strategy

We performed a systematic search of PubMed, Scopus, and Web of Science Core Collection from inception to June 2025, with no restrictions on language or publication year. The search strategy incorporated Medical Subject Headings (MeSH) and relevant free-text terms based on the PICO framework: Population (adults ≥18 years), Intervention (ashwagandha supplementation), Comparison (placebo), Outcomes (stress, anxiety, depression), and Study design (randomized controlled trials). The following search terms were used in various combinations: (“Ashwagandha” OR “Withania somnifera” OR “Indian ginseng” OR “winter cherry”) AND (“stress” OR “psychological stress” OR “mental stress” OR “anxiety” OR “generalized anxiety disorder” OR “depression” OR “depressive symptoms” OR “mood disorders”) AND (“randomized controlled trial” OR “RCT” OR “clinical trial” OR “intervention study” OR “placebo-controlled” OR “parallel-group” OR “double-blind”). Additionally, we manually screened the reference lists of all eligible studies and previous systematic reviews to ensure the inclusion of all relevant trials.

2.2. Study selection and eligibility criteria

Studies were included in the main analysis if they met the following criteria: (1) randomized controlled trial (RCT) design; (2) conducted on adults aged over 18 years; (3) reported outcomes related to mental health, including anxiety, stress, or depression, at both baseline and post-intervention for both the intervention and placebo groups; and (4) had an intervention duration of more than two weeks.

Studies were excluded if they met any of the following conditions: (1) duplicate publications; (2) absence of a placebo control group; (3) conducted on animals, children, or pregnant or breastfeeding women; (4) non-randomized study design; or (5) insufficient data for the outcomes of interest.

2.3. Data extraction

Two independent reviewers carried out the data extraction and study selection processes. From each eligible study, the following information was retrieved: first author’s surname, year of publication, participants’ age and gender, study location and duration, study design, ashwagandha dosage, sample size in each group, and the reported means and standard deviations (SDs) for anxiety, stress, and depression outcomes at baseline and after the intervention.

2.4. Risk of bias assessment

The risk of bias in the included studies was assessed using the Cochrane Risk of Bias Tool.[18]This tool evaluates potential sources of bias across several domains, including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other potential biases. Each domain was categorized as having low risk, some concerns, or high risk of bias. The assessments were independently performed by two reviewers, and discrepancies were resolved through discussion.

2.5. Certainty of evidence

The quality and certainty of evidence for each outcome were evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[19] This method assesses the strength of evidence based on five criteria: risk of bias, inconsistency, indirectness, imprecision, and potential publication bias. Each outcome was rated as having high, moderate, low, or very low certainty.

2.6. Statistical analysis

Effect sizes were calculated using the mean change and standard deviation (SD) for mental health outcomes (anxiety, stress, and depression) in both the ashwagandha and placebo groups. In cases where mean changes were not directly reported, they were estimated based on pre- and post-intervention data. When necessary, standard errors (SEs), 95 % confidence intervals (CIs), or interquartile ranges (IQRs) were converted to SDs using established methods.[20] If SDs for change scores were missing, they were computed using the following formula: $SD\_change = \sqrt{[(SD\_pre^2 + SD\_post^2) - (2 \times 0.9 \times SD\_pre \times SD\_post)]}$.[21] The pooled effect sizes were expressed as weighted mean differences (WMDs) with 95 % CIs and calculated using a random-effects model based on the DerSimonian and Laird method, accounting for between-study heterogeneity. Heterogeneity was assessed using the I^2 statistic and Cochrane’s Q test. Significant heterogeneity was defined as an I^2 value greater than 50 % or a p-value less than 0.05.[22,23] Prespecified subgroup analyses were conducted based on ashwagandha dosage (mg/day), duration of intervention (weeks), and participants’ baseline health status to explore potential sources of heterogeneity.

Sensitivity analyses were performed using the leave-one-out method to determine the influence of individual studies on the overall pooled estimate.[24] For crossover trials, appropriate adjustments were applied according to methods recommended by Elbourne et al.[25]

Publication bias was assessed using funnel plot asymmetry and Begg’s regression test. Additionally, meta-regression and nonlinear dose–response analyses using fractional polynomial models were performed to evaluate the relationship between ashwagandha dosage or intervention duration and the observed mental health outcomes.[26] All statistical analyses were conducted using Stata version 14 (Stata Corp, College Station, TX, USA), and p-values less than 0.05 were considered statistically significant.

3. Results

3.1. Study selection

The initial database search retrieved 3328 records. Following the

removal of 562 duplicates, 2766 unique studies remained for screening. Title and abstract assessment resulted in the exclusion of 2549 records deemed irrelevant to the research question. The full texts of the remaining 217 articles were then evaluated in detail. Of these, 143 randomized controlled trials (RCTs) were excluded for reporting outcomes outside the scope of this review. A further five studies were eliminated due to having an intervention period shorter than two weeks. Additionally, 35 RCTs were excluded because the intervention involved ashwagandha combined with other compounds exclusively in the treatment arm, and 12 trials were excluded for involving pediatric populations. In total, 22 RCTs satisfied all eligibility criteria and were included in the present systematic review and meta-analysis,[27–48] among which eleven studies assessed the impact of ashwagandha on stress,[29,31,32,35,41,43–48] seven studies on depression,[29,30,34,36,39,42,45] and fifteen studies on anxiety.[27–30,33,34,36–38,40–43,45,46] Fig. 1 illustrates the PRISMA flow diagram detailing the study selection process.

3.2. Characteristics of the included studies

Table 1 shows the characteristics of the 22 RCTs included in the current systematic review and meta-analysis. These RCTs were conducted in India,[27–29,32,35–38,40–43,45,46,48] USA,[30,31,34,39,44] Australia,[47] and Iran,[33] and were published between years 2000 and 2024. Only one study reported data on male and female separately,[44] and another studies reported male and female data together. The randomized controlled trials (RCTs) included in this review enrolled between 33 and 125 participants each, resulting in a combined sample of 1391 individuals. Participants' mean ages ranged from 23 to 54 years. Ashwagandha supplementation doses varied widely, from 60 mg/day to 12, 000 mg/day, with intervention periods lasting between 4 and 13 weeks. None of the included trials employed a cross-over design. In terms of supplement form, nine studies administered *Withania somnifera* extract as the intervention,[27,28,30,31,33,34,36,39,45] and thirteen studies administered ashwagandha root extract.[29,32,35,37,38,40–44,46–48] The included studies were conducted on patients with clinical stress,[27,29,32,35,45] insomnia,[37,38] bipolar disorder,[30] anxiety disorder,[28,33,36,42]

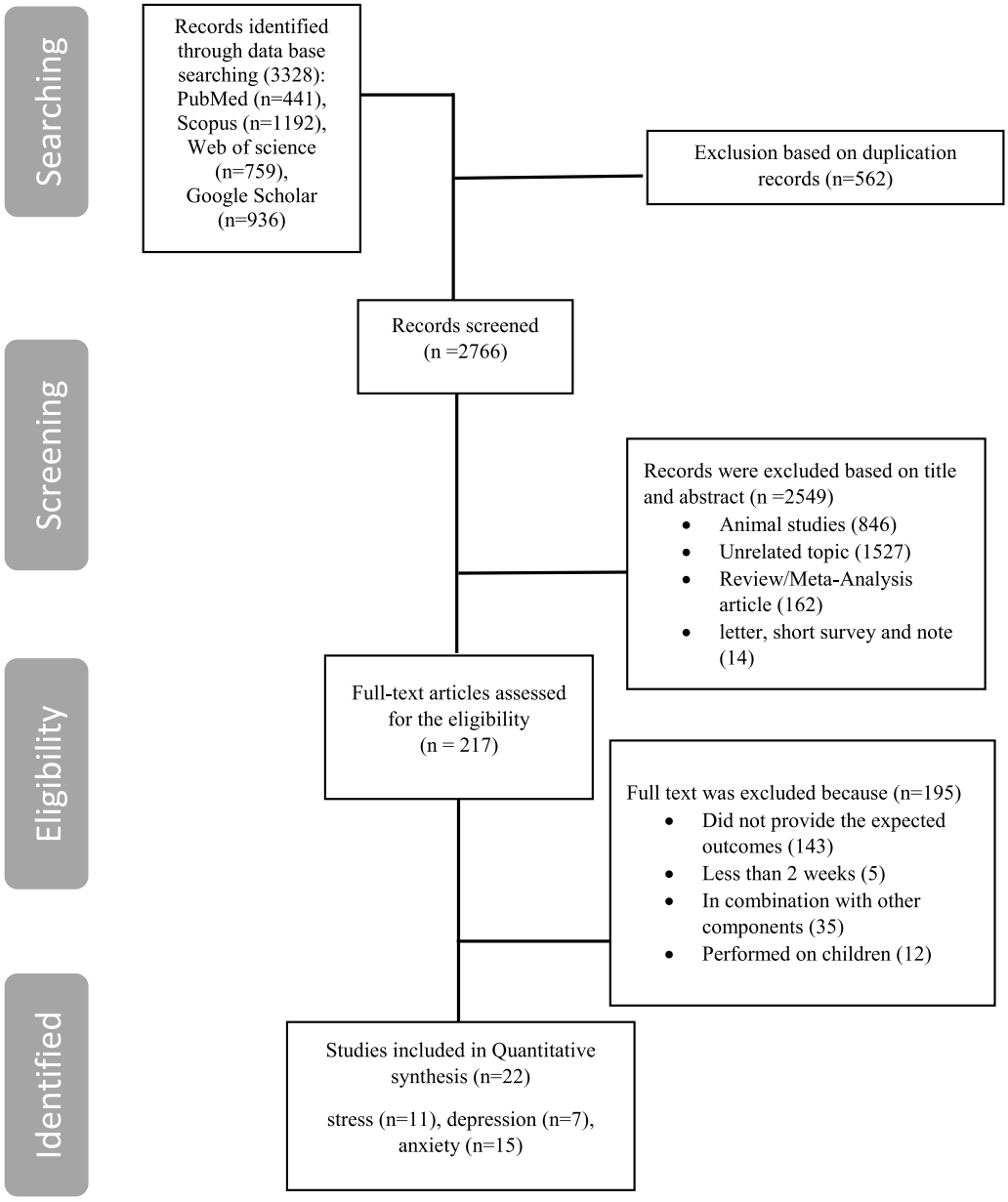

Fig. 1. Flow diagram of study selection.

Table 1
Characteristics of included studies.

Author, Year (Location)	Study design	Population	Gender	Number (Intervention/ control)	Intervention Mean (range) age (years)	Intervention Mean BMI (Kg/m2)	Duration (Weeks)	Intervention Intervention group Control group	Outcome	type of questionnaire
Abedon et al., 2008 (India) (a)	RCT, DB, Parallel	chronically stressed humans	M/F	19/15	37.8	-	8	Withania somnifera extract (WSE) (500 mg/day) Placebo	Anxiety	mHAM-A
Abedon et al., 2008 (India) (b)	RCT, DB, Parallel	chronically stressed humans	M/F	30/15	39.4	-	8	Withania somnifera extract (WSE) (250 mg/day) Placebo	Anxiety	mHAM-A
Abedon et al., 2008 (India) (c)	RCT, DB, Parallel	chronically stressed humans	M/F	34/15	40.0	-	8	Withania somnifera extract (WSE) (500 mg/day) Placebo	Anxiety	mHAM-A
Andrade et al., 2000 (India)	RCT, DB, Parallel	ICD-10 generalized anxiety disorder	M/F	17/16	41.9	-	6	ethanolic extract of Aswagandha (Withania somnifera) (500 mg/ day) Placebo	Anxiety	HAM-A
Chandrasekhar et al., 2012 (India) (a)	Prospective RCT, DB, Parallel	subjects with a history of chronic stress	M/F	30/31	25.8	-	8	Ashwagandha root extract (600 mg/day) placebo (neutral substance)	Anxiety Depression Stress Total	GHQ-28 DASS
Chandrasekhar et al., 2012 (India) (b)	Prospective RCT, DB, Parallel	subjects with a history of chronic stress	M/F	30/31	25.8	-	8	Ashwagandha root extract (600 mg/day) placebo (neutral substance)	Anxiety Depression Stress Total	DASS PSS
Chengappa et al., 2013 (USA)	RCT, DB, Parallel	bipolar disorder	M/F	24/29	46.9	-	8	Withania somnifera (WSE) (500 mg/day) placebo(inert substances or excipients)	Depression	MADRS
Chengappa et al., 2018 (USA)	RCT, DB, Parallel	schizophrenia or schizoaffective disorder	M/F	34/34	45.18	30.00	12	Withania somnifera (WSE) (1000 mg/day) Placebo	Stress	PSS
Choudhary et al., 2017 (India)	RCT, DB, Parallel	adults under chronic stress	M/F	25/25	-	26.88	8	Ashwagandha root extract (600 mg/day) Placebo	Stress	PSS
Gopukumar et al., 2021 (India)	RCT, DB, Parallel	Healthy and Stressed Adults	M/F	62/63	-	-	13	Ashwagandha SR (300 mg/day) Placebo	Stress	PSS
Khyati et al., 2013 (India)	RCT, DB, Parallel	Generalized Anxiety Disorder	M/F	44/42	-	-	8	Ashwagandha (Withania somnifera) (12000 mg/day) placebo(wheat flour)	Anxiety Depression	HAM-A
Langade et al., 2021 (India) (a)	RCT, DB, Parallel	healthy subjects	M/F	20/20	35.6	27.26	8	Ashwagandha root extract (600 mg/day) Placebo(starch)	Anxiety	HAM-A
Langade et al., 2021 (India) (b)	RCT, DB, Parallel	insomnia patients	M/F	20/20	38.70	27.15	8	Ashwagandha root extract (600 mg/day) Placebo(starch)	Anxiety	HAM-A
Langade et al., 2019 (India)	RCT, DB, Parallel	insomnia	M/F	39/19	38.83	26.91	10	Ashwagandha root extract (600 mg/day) Placebo(starch)	Anxiety	HAM-A
Lopresti et al., 2019 (India)	RCT, DB, Parallel	health adults	M/F	30/30	42.23	24.68	8	ashwagandha extract (240 mg/ day) Placebo(roasted rice powder)	Anxiety Total	HAM-A DASS
Salve et al., 2019 (India) (a)	Prospective RCT, DB, Parallel	health adults	M/F	19/19	29.65	-	8	Ashwagandha root extract (250 mg/day) Placebo(starch)	Anxiety Stress	HAM-A PSS

(*continued on next page*)

Table 1 (*continued*)

Author, Year (Location)	Study design	Population	Gender	Number (Intervention/ control)	Intervention Mean (range) age (years)	Intervention Mean BMI (Kg/m2)	Duration (Weeks)	Intervention Intervention group Control group	Outcome	type of questionnaire
Salve et al., 2019 (India) (b)	Prospective RCT, DB, Parallel	health adults	M/F	20/19	32.70	-	8	Ashwagandha root extract (600 mg/day) Placebo(starch)	Anxiety Stress	HAM-A PSS
Tiwari et al., 2021 (India)	Prospective RCT, DB, Parallel	healthy athletic adults	M/F	25/25	29.28	-	8	Ashwagandha root extract (600 mg/day) Placebo(starch)	Stress	RESTQ
Gannon et al., 2019 (USA)		schizophrenia	M/F	28/31	-	-	12	Withania somnifera (WSE) (1000 mg/day) Placebo	Anxiety Depression	PANSS
Leonard et al., 2024 (USA)		healthy volunteers	M/F	30/29	-	-	4	Withania somnifera (225 mg/ day) Placebo	Depression	POMS
Majeed et al., 2023 (India)		healthy adults	M/F	25/25	31.96	23.62	8	Ashwagandha root extract (500 mg/day) Placebo(Microcrystalline cellulose)	Anxiety Stress	GAD PSS
Majeed et al., 2024 (India)		adult with mental disorders	M/F	34/36	41.88	25.55	13	Ashwagandha root extract (500 mg/day) Placebo(Microcrystalline cellulose)	Anxiety Depression	HARS HDRS
Mishra et al., 2024 (India) (a)		healthy subjects with high stress levels	M/F	20/20	36.8	-	8	ashwagandha extract (60 mg/ day) Placebo(Microcrystalline cellulose)	Anxiety Stress	HAMA PSS
Mishra et al., 2024 (India) (b)			M/F	20/20	36.35	-	8	ashwagandha extract (120 mg/ day) Placebo(Microcrystalline cellulose)	Anxiety Stress	HAMA PSS
O'Connor et al., 2022 (USA) (a)			F	24/25	23.9	-	4	ashwagandha root (700 mg/day) Placebo	Stress	PSS
O'Connor et al., 2022 (USA) (b)			M	5/4	25.2	-	4	ashwagandha root (700 mg/day) Placebo	Stress	PSS
Pandit et al., 2024 (India) (a)			M/F	26/24	35.62	-	8	Withania somnifera (125 mg/ day) Placebo	Anxiety Depression Stress	HAM-A HAM-D PSS
Pandit et al., 2024 (India) (b)			M/F	26/24	35.38	-	8	Withania somnifera (250 mg/ day) Placebo	Anxiety Depression Stress	HAM-A HAM-D PSS
Pandit et al., 2024 (India) (c)			M/F	22/24	34.55	-	8	Withania somnifera (500 mg/ day) Placebo	Anxiety Depression Stress	HAM-A HAM-D PSS
Smith et al., 2023 (Australia)			M/F	55/56	53.72	30.00	12	ashwagandha root extract (400 mg/day) Placebo	Stress	PSS
Fuladi et al., 2020 (Iran)			M/F	18/22	39.89	-	6	Withania somnifera (1000 mg/ day) Placebo(lactose)	Anxiety	HAM-A

DB: double-blind; M: male; F: female; mHAM-A: modified Hamilton Anxiety Rating Scale; HAM-A: Hamilton Anxiety Rating Scale; GHQ-28: General Health Questionnaire – 28 items; DASS: Depression Anxiety Stress Scales; PSS: Perceived Stress Scale; MADRS: Montgomery–Åsberg Depression Rating Scale; RESTQ: Recovery–Stress Questionnaire; PANSS: Positive and Negative Syndrome Scale; POMS: Profile of Mood States; HARS: Hamilton Anxiety Rating Scale; HDRS: Hamilton Depression Rating Scale.

schizoaffective disorder,[31,34] overweight or mild obesity,[47] and healthy adults.[39–41,43,44,46,48]

3.3. Results from quality assessment

All included trials reported random sequence generation and blinding of participants and personnel, with both domains assessed as having a low risk of bias. Allocation concealment was not reported in three trials.[33,34,39] One trial was judged to have a high risk of bias in blinding outcome assessors.[48] For incomplete outcome data, most studies demonstrated a low risk of bias; however, two trials [34,36] had a high risk, and four studies [29,33,39,45] presented an unclear risk of attrition bias. Regarding selective outcome reporting, 20 studies were rated as having a low risk of bias (Table 2).

3.4. Meta-analysis and subgroup analysis

The pooled analysis indicated that ashwagandha supplementation significantly decreased stress (SMD = −5.88; 95 % CI: −8.15 to −3.60; $I^2 = 99.3$ %; Fig. 2), depression (SMD = −5.68; 95 % CI: −8.43 to −2.94; $I^2 = 99.7$ %; Fig. 3), and anxiety (SMD = −6.87; 95 % CI: −8.77 to −4.97; $I^2 = 99.9$ %; Fig. 4) across the included studies.

The subgroup analyses demonstrated that ashwagandha supplementation was associated with improvements in stress, depression, and anxiety across all examined categories (Table 3).

For stress, effect sizes were greater in trials administering lower daily doses (≤500 mg/day) compared with higher doses (>500 mg/day), while intervention duration exerted minimal influence. Participants with clinical psychological conditions exhibited larger effect sizes compared with those without clinical psychological conditions.

In depression, greater effect sizes were observed in studies using lower doses (≤500 mg/day) and in those with longer intervention durations (>8 weeks). Studies involving participants with pre-existing mental health disorders demonstrated more pronounced improvements than those conducted in healthy populations.

For anxiety, lower daily doses (≤500 mg/day) were associated with greater effect sizes, with negligible differences between shorter and longer interventions. Participants with psychological disorders demonstrated larger improvements than those without psychological disorders. Overall, these patterns suggest that lower daily doses and the presence of a baseline psychological disorder are associated with greater effect sizes, and that a longer intervention duration may further enhance the effects on depression; however, none of the between-subgroup differences were statistically significant.

3.5. Sensitivity analysis

The sensitivity analyses indicated that the exclusion of no individual study could statistically change the overall effect sizes for stress (95 % CI: −8.65 to −3.25), depression (95 % CI: −9.93 to −1.94), nor anxiety (95 % CI: −5.70 to −2.12).

3.6. Publication bias and trim-and-fill analysis

We used Egger's weighted regression test alongside visual inspection of funnel plots to assess publication bias in the included studies. The funnel plots revealed asymmetry for mental health outcomes, indicating potential publication bias (Supplementary Figure 1). Egger's test results confirmed the presence of publication bias for depression (P = 0.031), stress (P = 0.003), and anxiety (P = 0.017). Therefore, we conducted a trim-and-fill analysis to estimate the impact of potentially missing studies. No hypothetical studies were added by this method, and the overall effect sizes for mental health outcomes remained unchanged.

3.7. Non-linear dose-response association between duration and dosage of ashwagandha supplementation and mental health

As shown in Fig. 5, the non-linear dose–response analysis indicated a significant association between supplementation dosage and stress levels (P-nonlinearity = 0.005), whereas no such associations were

Table 2
Results of risk of bias assessment for randomized clinical trials included in the current meta-analysis.

Study	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other potential threats to validity
Abedon et al. 2008	L	L	L	L	L	L	U
Andrade et al. 2000	L	L	L	L	L	L	U
Chandrasekhar et al. 2012	L	L	L	L	U	L	U
Chengappa et al. 2013	L	L	L	L	L	L	U
Chengappa et al. 2018	L	L	L	L	L	L	U
Choudhary et al. 2017	L	L	L	L	L	L	U
Gopukumar et al. 2021	L	L	L	L	L	U	U
Khyati et al. 2013	L	L	L	L	H	L	U
Langade et al. 2021	L	L	L	L	L	L	U
Langade et al. 2019	L	L	L	L	L	L	U
Lopresti et al. 2019	L	L	L	L	L	L	U
Salve et al. 2019	L	L	L	L	L	L	U
Tiwari et al. 2021	L	L	L	U	L	L	U
Gannon et al. 2019	L	U	L	L	H	U	U
Leonard et al. 2024	L	U	L	L	U	L	U
Majeed et al. 2023	L	L	L	L	L	L	U
Majeed et al. 2024	L	L	L	L	L	L	U
Mishra et al. 2024	L	L	L	L	L	L	U
O'Connor et al. 2022	L	L	L	L	L	L	U
Pandit et al. 2024	L	L	L	L	U	L	U
Smith et al. 2023	L	L	L	L	L	L	U
Fuladi et al. 2020	L	U	L	L	U	L	U

H: high risk of bias, L: low risk of bias, U: unknown risk of bias.

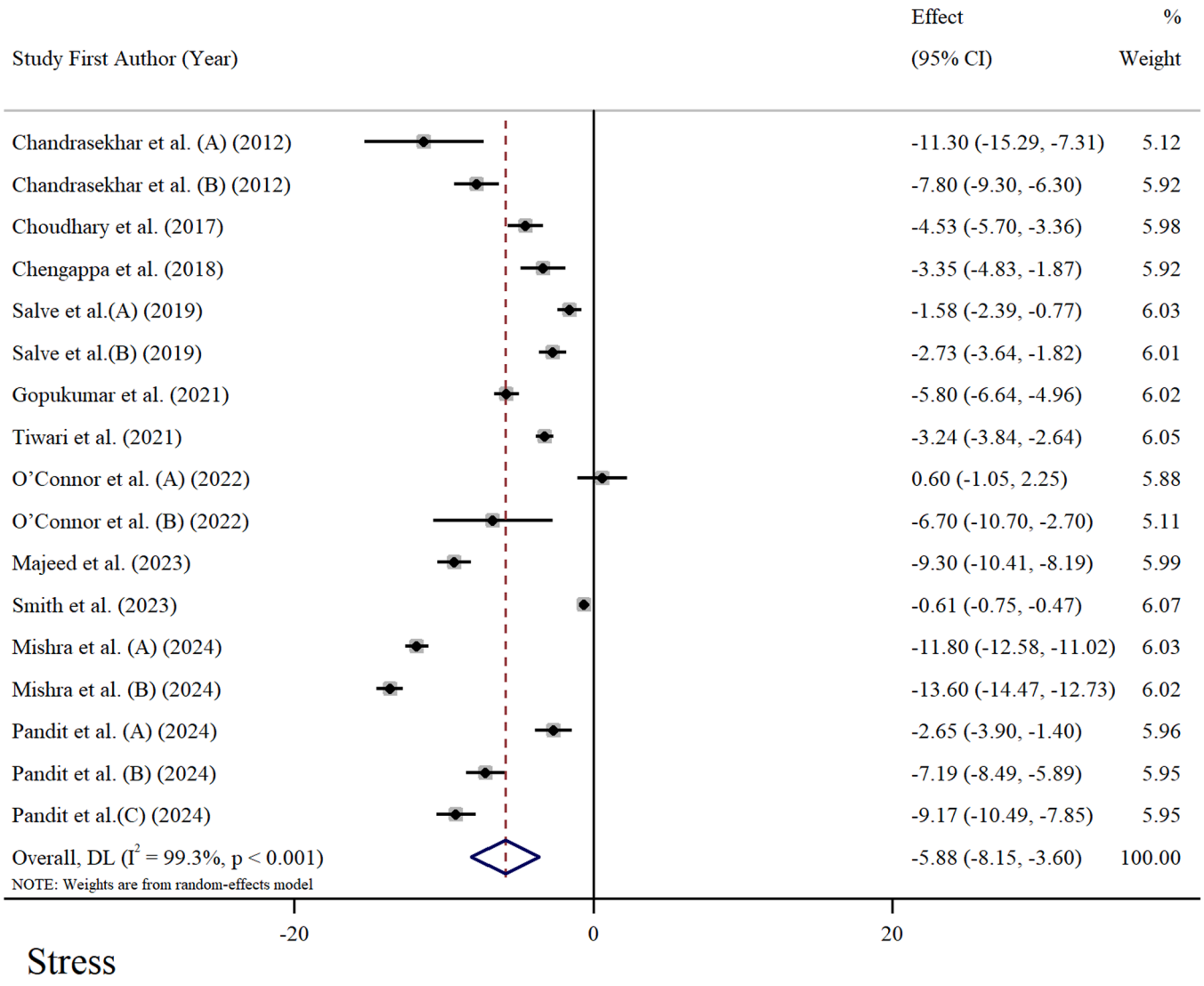

Fig. 2. Forest plots for the effect of ashwagandha supplementation on stress. Horizontal lines represent 95 % CIs. Diamonds represent pooled estimates from random-effects analysis. WMD: weighted mean difference, CI: confidence interval.

found for anxiety (P-nonlinearity = 0.336) or depression (P-nonlinearity = 0.221). Similarly, the duration of the interventions was not significantly related to stress (P-nonlinearity = 0.313), anxiety (P-nonlinearity = 0.714), or depression (P-nonlinearity = 0.626).

3.8. Meta-regression analysis

A meta-regression analysis was conducted to examine the linear associations between supplementation dose and duration with mental health indices. A significant positive association was identified between dosage and stress levels (coefficient = 0.005, P = 0.031). In contrast, no significant dose-related associations were observed for anxiety (coefficient = 0.17, P = 0.206) or depression (coefficient = 0.006, P = 0.083). Moreover, the effects of ashwagandha supplementation on mental health outcomes were not influenced by the duration of the interventions, as evidenced by the non-significant associations for anxiety (coefficient = 1.23, P = 0.637), stress (coefficient = 0.005, P = 0.985), and depression (coefficient = –0.511, P = 0.347).

3.9. Grading of evidence

The GRADE guidelines were applied to assess the quality of evidence across the included studies at the outcome level. The quality of evidence was ranked as very low regarding to anxiety, stress, and depression (Supplementary Table 1).

4. Discussion

The findings of the present systematic review and meta-analysis suggest that supplementation with ashwagandha could ameliorate symptoms of stress, anxiety, and depression in individuals with various health status. The subgroup analyses also reiterated these observations by showing statistical significance across all subgroups. The meta-regression analysis indicated a direct association between the dosage of administration of ashwagandha and amelioration in stress levels; however, no such association was observed for other outcomes. Likewise, we observed a non-linear dose-response association between dosage of ashwagandha and stress levels. We were not able to detect any non-linear associations between dosage/duration of the interventions and the improvement of indices regarding anxiety or depression.

The existing literature supports the anti-anxiety and anti-stress effects of ashwagandha, almost unilaterally. For instance, Bachour et al. [49] reported that an eight-week supplementation with ashwagandha significantly improves anxiety (measured by the Hamilton Anxiety Rating Scale (HAM-A)), perceived stress (measured by Perceived Stress Scale (PSS)), and cortisol levels in patients with stress and/or anxiety.

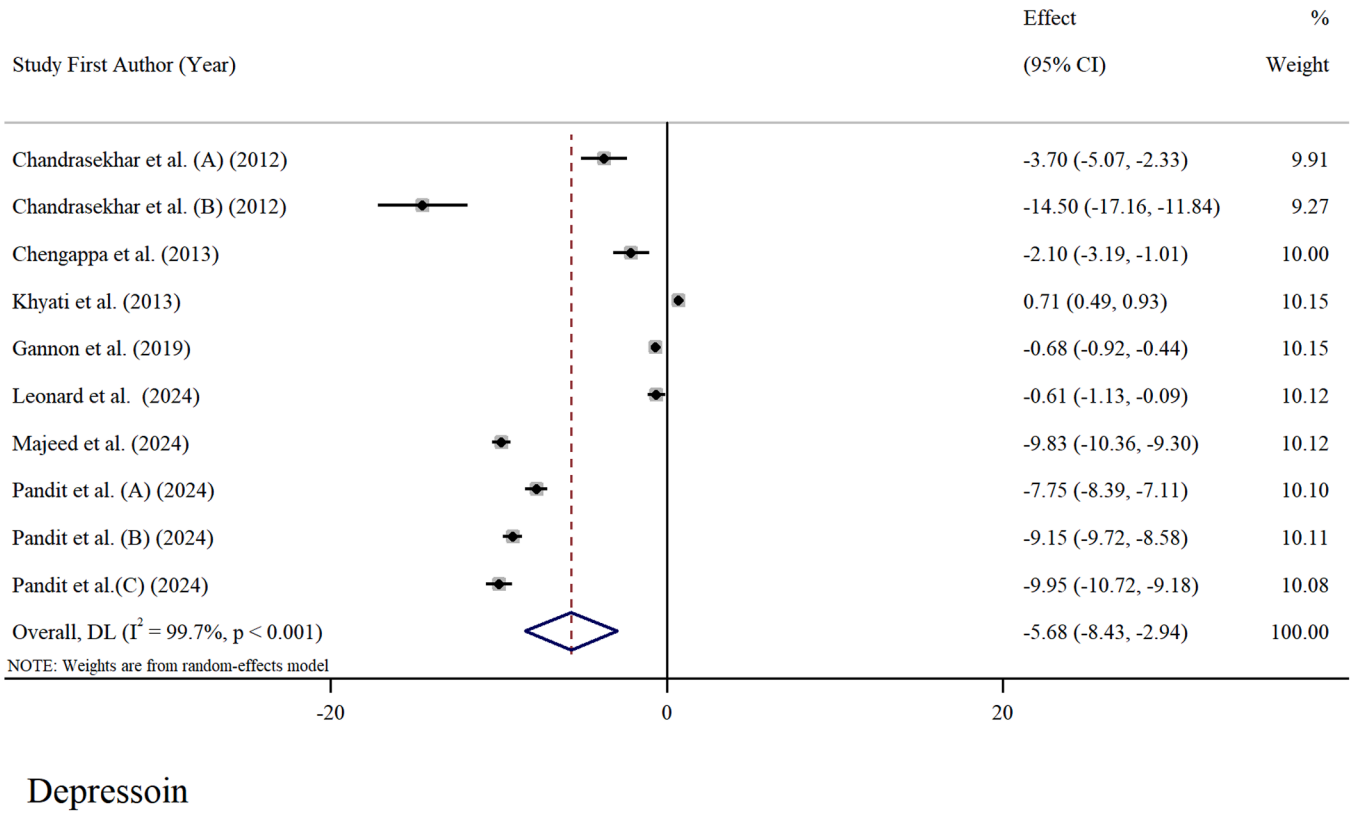

Fig. 3. Forest plots for the effect of ashwagandha supplementation on depression. Horizontal lines represent 95 % CIs. Diamonds represent pooled estimates from random-effects analysis. WMD: weighted mean difference, CI: confidence interval.

Likewise, Arumugam et al. [15] reported that ashwagandha significantly improves HAM, PSS, and serum cortisol levels in study subjects. Nonetheless, contrasting evidence have challenged the impact of such intervention in effectively reducing psychological stress. For instance, in a systematic review and meta-analysis, Albalawi et al. [50] observed that while ashwagandha supplementation significantly reduced cortisol levels, it did not produce a significant improvement in perceived stress scores (PSS). Such discrepancies might be caused by variations in study subjects included and other methodological differences. Nevertheless, Della Porta et al. [51] have argued that since the circadian rhythm of cortisol secretion and meal-induced cortisol release are not controlled in the majority of studies, changes in cortisol levels cannot be solely attributed to supplementation with the herb. Our findings suggest that health status of participants might not be a relevant factor to determine the effectiveness of the treatment—the subgroup analysis included both healthy and unhealthy individuals many of whom have been diagnosed with clinical stress and anxiety disorder. However, we were not able to empirically verify the existence of a system to control for such sources of possible confounding in the included studies.

Intervention with ashwagandha seems to target stress-regulating pathways, most prominently hypothalamic-pituitary-adrenal (HPA) axis,[14] mainly through its abundance in various potent withanolides, as well as several alkaloids and flavonoids.[52] These bioactive compounds have also been linked to enhancements in GABAergic and serotonergic pathways which have been associated with the herb's potential to improve sleep duration, quality, and latency.[53] Improved sleep quality might then act as a mediator between the intervention and improved stress levels in individuals.[54]

Depression is a prevalent mental disorder, with various physiological and societal factors suggested as possible underlying causes,.[55] Multiple interventions, from psychotherapy to neurotransmitter-modifying medications have been used to improve the mood imbalance in patients with major depression.[56] Imbalances in GABAergic, glutamatergic, serotonergic, and monoaminergic signaling systems have been proposed as the most likely mechanisms to be involved with the symptoms of the disease.[57] Moreover, the increased production of reactive oxygen species (ROSs) in the brain have been suggested as a probable cause for depressive disorders.[58]

Besides standard approaches, treatment with medicinal herbs, such as ashwagandha, have been claimed to improve indices of depressive mood modifications.[59,60] Several pathways, including the inhibition of production of ROSs and its possible function in maintaining serotonin levels in the brain, have been proposed as potential mechanisms through which ashwagandha could ameliorate depressive symptoms in patients.[61] Although the findings of the present study suggest favorable indication for the use of the herb, some factors need to be taken into account. Firstly, the serotonin theory of depression is being seriously questioned.[62] In other words, depression is a complex issue with many players at harmony; thus, a more comprehensive approach must be adopted when dealing with patients. Secondly, even though ashwagandha is regarded as safe in high doses,[63] issues of safety must be considered, especially in those with chronic conditions who may need to consume herbal products for longer periods of time. Finally, none of the included studies enrolled patients with clinical major depression which restricts generalizability to those with the condition.

The present systematic review and meta-analysis is unprecedented in investigating the impact of ashwagandha on three major mood disorders. However, there are some limitations. Firstly, the scores/indices by which the status of participants was assessed, were vastly heterogenous. Thus, measurement bias should not be disregarded. Secondly, included studies were significantly heterogenous. Subgroup analyses were conducted to further investigate the sources of heterogeneity. Thirdly, we also observed publication bias for all three major outcomes. Fourthly, included studies were assessed to have very low quality for all three major outcomes. Finally, we could not detect any linear/non-linear associations between the dosage/duration of intervention and the impact

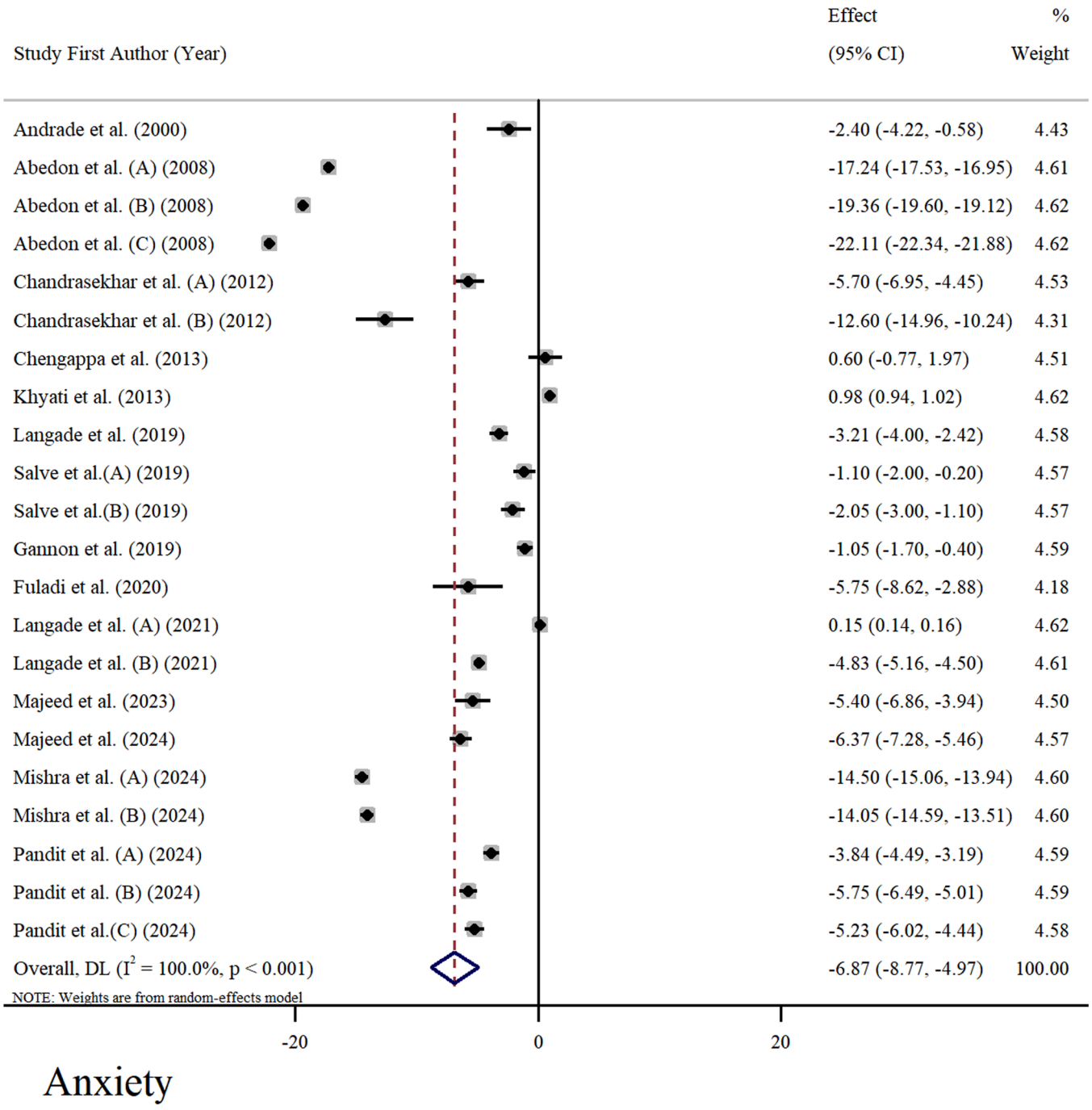

Fig. 4. Forest plots for the effect of ashwagandha supplementation on anxiety. Horizontal lines represent 95 % CIs. Diamonds represent pooled estimates from random-effects analysis. WMD: weighted mean difference, CI: confidence interval.

of supplementation on anxiety nor depression. Based on these observations, further research needs to be conducted to illuminate the effective dosages/duration for each outcome.

5. Conclusion

This systematic review and dose–response meta-analysis provides the most comprehensive synthesis of randomized controlled trials on ashwagandha (*Withania somnifera*) supplementation to date, including novel linear and non-linear dose–response analyses. Our findings suggest that ashwagandha supplementation may help reduce symptoms of stress, anxiety, and depression in adults. Importantly, the observed dose–response relationship for stress highlights the potential relevance of dosage in shaping clinical outcomes. However, the certainty of evidence was rated as very low, primarily due to significant heterogeneity, publication bias, and variability in outcome measures. Consequently, these results should be interpreted with caution. Ashwagandha should not yet be regarded as a definitive treatment option but rather as a promising complementary strategy that warrants further investigation. Future high-quality, standardized, and longer-term RCTs are essential to establish optimal dosing, treatment duration, and applicability across different populations.

Ethical approval

Ethical approval was not required for this secondary analysis.

Table 3
Subgroup analysis to assess the effect of ashwagandha on mental health outcomes.

Variable	Number of effect sizes	SMD (95 % CI)	P-value[1]	I^2 (%)[2]	P-heterogeneity[3]	P-between subgroup heterogeneity[4]
Stress						
Overall	17	-5.88 (-8.15, −3.60)	< 0.001	99.3	< 0.001	-
Dosage (mg/day)						< 0.001
≤ 500	9	-2.25 (-2.48, −2.02)	< 0.001	94.5	< 0.001	
>500	8	-1.47 (-1.70, −1.23)	< 0.001	89.4	< 0.001	
Duration (weeks)						0.174
≤ 8	14	-1.96 (-2.17, −1.75)	< 0.001	94.0	< 0.001	
> 8	3	-1.72 (-1.99, −1.45)	< 0.001	86.8	< 0.001	
Presence of psychological disorders						0.007
Yes	6	-1.49 (-1.83, −1.16)	< 0.001	94.0	< 0.001	
No	11	-2.00 (-2.19, −1.81)	< 0.001	93.0	< 0.001	
Depression						
Overall	10	-5.68 (-8.43, −2.94)	< 0.001	99.7	< 0.001	-
Dosage (mg/day)						< 0.001
≤ 500	6	-2.11 (-2.46, −1.78)	< 0.001	98.0	< 0.001	
>500	4	-0.62 (-0.90, −0.34)	< 0.001	97.5	< 0.001	
Duration (weeks)						< 0.001
≤ 8	8	-0.99 (-1.22, −0.75)	< 0.001	97.8	< 0.001	
> 8	2	-2.33 (-2.87, −1.80)	< 0.001	98.7	< 0.001	
Presence of psychological disorders						0.011
Yes	1	-0.59 (-1.17, −0.07)	0.026	-	-	
No	9	-1.34 (-1.58, −1.10)	< 0.001	98.0	< 0.001	
Anxiety						
Overall	22	-6.87 (-8.77, −4.97)	< 0.001	99.9	< 0.001	-
Dosage (mg/day)						< 0.001
≤ 500	13	-1.94 (-2.20, −1.68)	< 0.001	97.5	< 0.001	
>500	9	-1.23 (-1.49, −0.98)	< 0.001	97.9	< 0.001	
Duration (weeks)						0.144
≤ 8	19	-1.51 (-1.71, −1.30)	< 0.001	97.8	< 0.001	
> 8	3	-1.82 (-2.18, −1.45)	< 0.001	93.4	< 0.001	
Presence of psychological disorders						0.014
Yes	5	-1.23 (-1.56, −0.90)	< 0.001	96.2	< 0.001	
No	17	-1.73 (-1.94, −1.40)	< 0.001	97.9	< 0.001	

SMD: standardized mean difference; CI: confidence interval.
[1]Refers to the SMD (95 % CI).
[2]Indicates between-study heterogeneity (as percentage).
[3]Obtained from the Q-test.
[4]Obtained from the fixed-effect model.

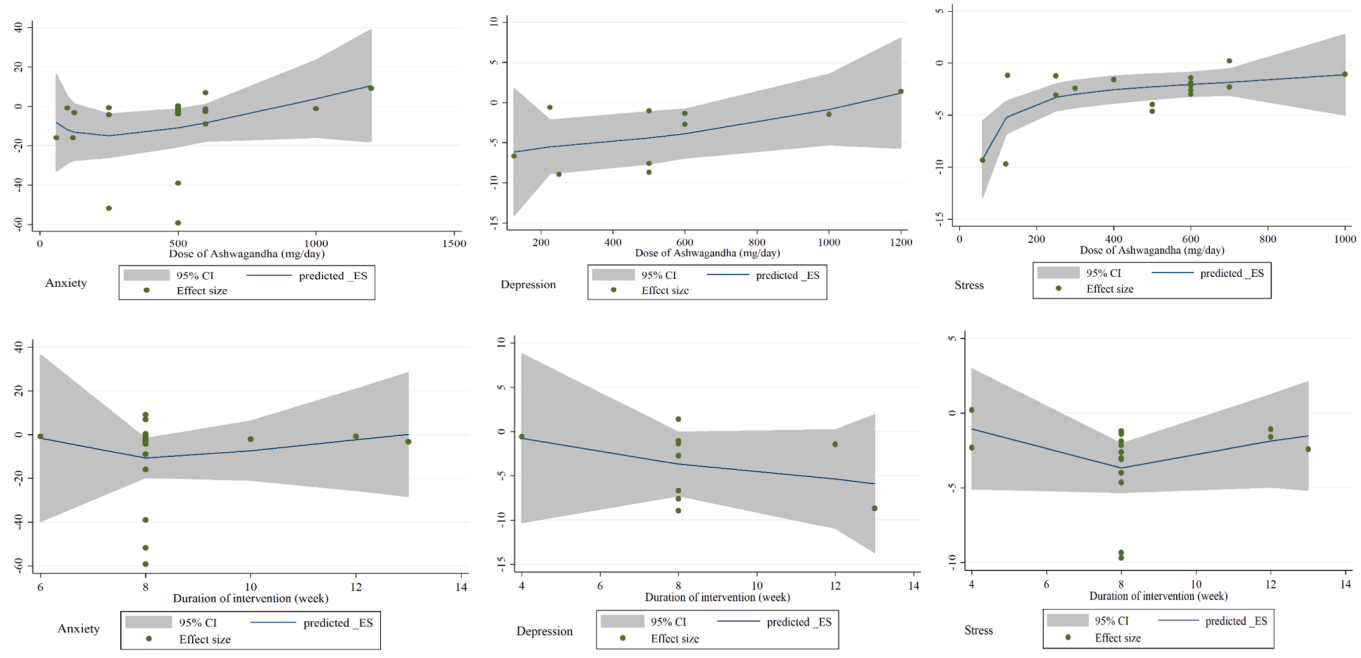

Fig. 5. Dose-response relations between ashwagandha supplementation dosage (mg/day) and duration of intervention (week) with absolute (unstandardized) mean differences of the outcomes in nonlinear fashion.

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CRediT authorship contribution statement

Moein Askarpour: Writing – review & editing, Writing – original draft, Supervision, Software, Methodology, Investigation, Funding acquisition, Conceptualization. **Saleh A. Alsanie:** Writing – original draft, Methodology, Conceptualization. **Fahad Saad Alhodieb:** Writing – original draft, Methodology, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ctim.2026.103325.

References

1. Lubecka B, Lubecki M, Pudlo R. Epidemiology of anxiety and depressive disorders. *Psychiatria*. 2022;19(1):66–77. Available from: ⟨https://ppm.sum.edu.pl/info/article/SUM3199116ceb1e4ef5be5baf4387412752⟩.
2. Javaid SF, Hashim IJ, Hashim MJ, Stip E, Samad MA, Ahbabi AA. Epidemiology of anxiety disorders: global burden and sociodemographic associations. *Middle East Curr Psychiatry*. 2023;30(1):44. https://doi.org/10.1186/s43045-023-00315-3.
3. Zhu C, Zhang T, Li Q, Chen X, Wang K. Depression and anxiety during the COVID-19 pandemic: epidemiology, mechanism, and treatment. *Neurosci Bull*. 2023;39(4):675–684. https://doi.org/10.1007/s12264-022-00970-2.
4. Mazza MG, Palladini M, Poletti S, Benedetti F. Post-COVID-19 depressive symptoms: epidemiology, pathophysiology, and pharmacological treatment. *CNS Drugs*. 2022;36(7):681–702. https://doi.org/10.1007/s40263-022-00931-3.
5. Yang J-s, Zhang L-y, Yang C-h, Li X-y, Li Z-q. Global, regional, and national epidemiology of depression in working-age individuals, 1990–2019. *Depress Anxiety*. 2024;2024(1), 4747449. https://doi.org/10.1155/2024/4747449.
6. Marwaha S, Palmer E, Suppes T, Cons E, Young AH, Upthegrove R. Novel and emerging treatments for major depression. *Lancet*. 2023;401(10371):141–153. https://doi.org/10.1016/S0140-6736(22)02080-3.
7. Szuhany KL, Simon NM. Anxiety disorders: a review. *Jama*. 2022;328(24):2431–2445. https://doi.org/10.1001/jama.2022.22744.
8. Gaurav H, Yadav D, Maurya A, et al. Biodiversity, biochemical profiling, and pharmaco-commercial applications of Withania somnifera: a review. *Molecules*. 2023;28(3):1208. https://doi.org/10.3390/molecules28031208.
9. Paul S, Chakraborty S, Anand U, et al. Withania somnifera (L.) Dunal (Ashwagandha): a comprehensive review on ethnopharmacology, pharmacotherapeutics, biomedicinal and toxicological aspects. *Biomed Pharmacother*. 2021;143, 112175. https://doi.org/10.1016/j.biopha.2021.112175.
10. Mikulska P, Malinowska M, Ignacyk M, et al. Ashwagandha (Withania somnifera)—current research on the health-promoting activities: a narrative review. *Pharmaceutics*. 2023;15(4):1057. https://doi.org/10.3390/pharmaceutics15041057.
11. Guo S, Rezaei MJ. The benefits of ashwagandha (Withania somnifera) supplements on brain function and sports performance. *Front Nutr*. 2024;11, 1439294. https://doi.org/10.3389/fnut.2024.1439294.
12. Syed AA, Reza MI, Singh P, Thombre GK, Gayen JR. Withania somnifera in Neurological Disorders: Ethnopharmacological Evidence, Mechanism of Action and its Progress in Delivery Systems. *Curr Drug Metab*. 2021;22(7):561–571. https://doi.org/10.2174/1389200222666210203182716.
13. Hasler G. Pathophysiology of depression: do we have any solid evidence of interest to clinicians? *World Psychiatry J World Psychiatr Assoc (WPA)*. 2010;9(3):155–161. https://doi.org/10.1002/j.2051-5545.2010.tb00298.x.
14. Akhgarjand C, Asoudeh F, Bagheri A, et al. Does Ashwagandha supplementation have a beneficial effect on the management of anxiety and stress? A systematic review and meta-analysis of randomized controlled trials. *Phytother Res PTR*. 2022;36(11):4115–4124. https://doi.org/10.1002/ptr.7598.
15. Arumugam V, Vijayakumar V, Balakrishnan A, et al. Effects of Ashwagandha (Withania somnifera) on stress and anxiety: A systematic review and meta-analysis. *Explor (N Y NY)*. 2024;20(6), 103062. https://doi.org/10.1016/j.explore.2024.103062.
16. Fatima K, Malik J, Muskan F, et al. Safety and efficacy of Withania somnifera for anxiety and insomnia: Systematic review and meta-analysis. *Hum Psychopharmacol*. 2024;39(6), e2911. https://doi.org/10.1002/hup.2911.
17. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. https://doi.org/10.1136/bmj.n71.
18. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928. https://doi.org/10.1136/bmj.d5928.
19. Falck-Ytter Y, Guyatt G, Vist G, Kunz R. Rating quality of evidence and strength of recommendations GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336:924–926. https://doi.org/10.1136/bmj.39489.470347.AD.
20. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol*. 2005;5:13. https://doi.org/10.1186/1471-2288-5-13.
21. Rosenblad A. Introduction to meta-analysis by Michael Borenstein, Larry V. Hedges, Julian P.T. Higgins, Hannah R. Rothstein. *Int Stat Rev*. 2009;77(3):478–479. https://doi.org/10.1111/j.1751-5823.2009.00095_15.x.
22. Brondani LA, Assmann TS, de Souza BM, Boucas AP, Canani LH, Crispim D. Meta-analysis reveals the association of common variants in the uncoupling protein (UCP) 1-3 genes with body mass index variability. *PloS One*. 2014;9(5), e96411. https://doi.org/10.1371/journal.pone.0096411.
23. Zahedi H, Djalalinia S, Sadeghi O, et al. Dietary inflammatory potential score and risk of breast cancer: systematic review and meta-analysis. *Clin Breast Cancer*. 2018;18(4):e561–e570. https://doi.org/10.1016/j.clbc.2018.01.007.
24. Tobias A. Assessing the influence of a single study in the meta-analysis estimate. *Stata Tech Bull*. 1999;47:15–17. ⟨https://ideas.repec.org/a/tsj/stbull/y1999v8i47sbe26.html⟩ (Availabe from).
25. Elbourne DR, Altman DG, Higgins JP, Curtin F, Worthington HV, Vail A. Meta-analyses involving cross-over trials: methodological issues. *Int J Epidemiol*. 2002;31(1):140–149. https://doi.org/10.1093/ije/31.1.140.
26. Foster G. Interpreting and visualizing regression models using stata, by Michael N. Mitchell (Stata Press, College Station, Texas, 2012), pp. xxix + 558. *Econ Rec*. 2013;89(284):132–134. https://doi.org/10.1111/1475-4932.12023.
27. Abedon B, Auddy B, Hazra J, Mitra A, Ghosal S. A standardized Withania somnifera extract significantly reduces stress-related parameters in chronically stressed humans: a double-blind, randomized, placebo-controlled study. *Jana*. 2008;11:50–56. Available from:⟨https://www.semanticscholar.org/paper/A-Standardized-Withania-Somnifera-Extract-Reduces-A-Auddy-Hazra/46bdaebfcf4f00730ad217fd6bb88228964e4c2e⟩.
28. Andrade C, Aswath A, Chaturvedi S, Srinivasa M, Raguram R. A double-blind, placebo-controlled evaluation of the anxiolytic efficacy ff an ethanolic extract of Withania somnifera. *Indian J Psychiatry*. 2000;42(3):295–301. ⟨https://pubmed.ncbi.nlm.nih.gov/21407960⟩.
29. Chandrasekhar K, Kapoor J, Anishetty S. 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 J Psychol Med*. 2012;34(3):255–262. https://doi.org/10.4103/0253-7176.106022.
30. Chengappa KR, Bowie CR, Schlicht PJ, Fleet D, Brar JS, Jindal R. Randomized placebo-controlled adjunctive study of an extract of Withania somnifera for cognitive dysfunction in bipolar disorder. *J Clin Psychiatry*. 2013;74(11):16816. https://doi.org/10.4088/JCP.13m08413.
31. Chengappa KR, Brar JS, Gannon JM, Schlicht PJ. Adjunctive use of a standardized extract of Withania somnifera (Ashwagandha) to treat symptom exacerbation in schizophrenia: a randomized, double-blind, placebo-controlled study. *J Clin Psychiatry*. 2018;79(5):22496. https://doi.org/10.4088/JCP.17m11826.
32. Choudhary D, Bhattacharyya S, Joshi K. Body weight management in adults under chronic stress through treatment with ashwagandha root extract: a double-blind, randomized, placebo-controlled trial. *J EvidBased Complement Altern Med*. 2017;22(1):96–106. https://doi.org/10.1177/2156587216641830.
33. Fuladi S, Emami S, Mohammadpour A, Karimani A, Manteghi A, Sahebkar A. Assessment of Withania somnifera root extract efficacy in patients with generalized anxiety disorder: a randomized double-blind placebo-controlled trial [published online ahead of print, 2020 Apr 13]. *Curr Clin Pharm*. 2020:10. https://doi.org/10.2174/1574884715666200413120413.
34. Gannon JM, Brar J, Rai A, Chengappa KR. Effects of a standardized extract of Withania somnifera (Ashwagandha) on depression and anxiety symptoms in persons with schizophrenia participating in a randomized, placebo-controlled clinical trial. *Ann Clin Psychiatry*. 2019;31(2):123–129. ⟨https://pubmed.ncbi.nlm.nih.gov/31046033⟩.
35. Gopukumar K, Thanawala S, Somepalli V, Rao TS, Thamatam VB, Chauhan S. Efficacy and safety of ashwagandha root extract on cognitive functions in healthy, stressed adults: a randomized, double-blind, placebo-controlled study. *Evid-Based Complement Altern Med*. 2021;2021(1), 8254344. https://doi.org/10.1155/2021/8254344.
36. Khyati S, Anup B. A randomized double blind placebo controlled study of ashwagandha on generalized anxiety disorder. *Int Ayurvedic Med J*. 2013;1:1–7. Available from: ⟨https://www.iamj.in/images/upload/01.05.14_IAMJ.pdf⟩.

37. Langade D, Kanchi S, Salve J, Debnath K, Ambegaokar D, Langade DG. Efficacy and safety of Ashwagandha (Withania somnifera) root extract in insomnia and anxiety: a double-blind, randomized, placebo-controlled study. *Cureus*. 2019;11(9). https://doi.org/10.7759/cureus.5797.
38. Langade D, Thakare V, Kanchi S, Kelgane S. Clinical evaluation of the pharmacological impact of ashwagandha root extract on sleep in healthy volunteers and insomnia patients: a double-blind, randomized, parallel-group, placebo-controlled study. *J Ethnopharmacol*. 2021;264, 113276. https://doi.org/10.1016/j.jep.2020.113276.
39. Leonard M, Dickerson B, Estes L, et al. Acute and repeated ashwagandha supplementation improves markers of cognitive function and mood. *Nutrients*. 2024;16(12):1813. https://doi.org/10.3390/nu16121813.
40. Lopresti AL, Smith SJ, Malvi H, Kodgule R. An investigation into the stress-relieving and pharmacological actions of an ashwagandha (Withania somnifera) extract: a randomized, double-blind, placebo-controlled study. *Medicine*. 2019;98(37), e17186. https://doi.org/10.1097/MD.0000000000017186.
41. Majeed M, Nagabhushanam K, Mundkur L. A standardized Ashwagandha root extract alleviates stress, anxiety, and improves quality of life in healthy adults by modulating stress hormones: results from a randomized, double-blind, placebo-controlled study. *Medicine*. 2023;102(41), e35521. https://doi.org/10.1097/MD.0000000000035521.
42. Majeed M, Nagabhushanam K, Murali A, Vishwanathan DT, Mamidala RV, Mundkur L. A standardized Withania somnifera (Linn.) root extract with piperine alleviates the symptoms of anxiety and depression by increasing serotonin levels: a double-blind, randomized, placebo-controlled study. *J Integr Complement Med*. 2024;30(5):459–468. https://doi.org/10.1089/jicm.2023.0279.
43. Mishra DN, Kumar M. Shoden promotes Relief from stress and anxiety: a randomized, double-blind, placebo-controlled study on healthy subjects with high stress levels. *Heliyon*. 2024;10(17). https://doi.org/10.1016/j.heliyon.2024.e36885.
44. O'Connor J, Lindsay K, Baker C, Kirby J, Hutchins A, Harris M. The impact of ashwagandha on stress, sleep quality, and food cravings in college students: quantitative analysis of a double-blind randomized control trial. *J Med Food*. 2022;25(12):1086–1094. https://doi.org/10.1089/jmf.2022.0040.
45. Pandit S, Srivastav AK, Sur TK, Chaudhuri S, Wang Y, Biswas TK. Effects of withania somnifera extract in chronically stressed adults: a randomized controlled trial. *Nutrients*. 2024;16(9):1293. https://doi.org/10.3390/nu16091293.
46. Salve J, Pate S, Debnath K, Langade D, Langade DG. Adaptogenic and anxiolytic effects of ashwagandha root extract in healthy adults: a double-blind, randomized, placebo-controlled clinical study. *Cureus*. 2019;11(12). https://doi.org/10.7759/cureus.6466.
47. Smith SJ, Lopresti AL, Fairchild TJ. Exploring the efficacy and safety of a novel standardized ashwagandha (Withania somnifera) root extract (Witholytin®) in adults experiencing high stress and fatigue in a randomized, double-blind, placebo-controlled trial. *J Psychopharmacol*. 2023;37(11):1091–1104. https://doi.org/10.1177/02698811231200023.
48. Tiwari S, Gupta SK, Pathak AK. A double-blind, randomized, placebo-controlled trial on the effect of Ashwagandha (Withania somnifera dunal.) root extract in improving cardiorespiratory endurance and recovery in healthy athletic adults. *J Ethnopharmacol*. 2021;272, 113929. https://doi.org/10.1016/j.jep.2021.113929.
49. Bachour G, Samir A, Haddad S, Houssaini MA, El Radad M. Effects of ashwagandha supplements on cortisol, stress, and anxiety levels in adults: a systematic review and meta-analysis. S39-S39 *BJPsych Open*. 2025;11(S1). https://doi.org/10.1192/bjo.2025.10136.
50. Albalawi AA. Dual impact of ashwagandha: significant cortisol reduction but no effects on perceived stress – a systematic review and meta-analysis. *Nutr Health*. 2025;0(0). https://doi.org/10.1177/02601060251363647.
51. Della Porta M, Maier JA, Cazzola R. Effects of Withania somnifera on cortisol levels in stressed human subjects: a systematic review. *Nutrients*. 2023;15(24):5015. https://doi.org/10.3390/nu15245015.
52. Shinde S, Balasubramaniam AK, Mulay V, Saste G, Girme A, Hingorani L. Recent advancements in extraction techniques of ashwagandha (withania somnifera) with insights on phytochemicals, structural significance, pharmacology, and current trends in food applications. *ACS Omega*. 2023;8(44):40982–41003. https://doi.org/10.1021/acsomega.3c03491.
53. Grabowski WK, Karoń KA, Karoń ŁM, et al. Unlocking better sleep and stress relief: the power of ashwagandha (withania somnifera) supplementation–a literature review. -54904 *Qual Sport*. 2024;26:54904. https://doi.org/10.12775/QS.2024.26.54904.
54. Martire VL, Caruso D, Palagini L, Zoccoli G, Bastianini S. Stress & sleep: a relationship lasting a lifetime. *Neurosci Biobehav Rev*. 2020;117:65–77. https://doi.org/10.1016/j.neubiorev.2019.08.024.
55. Nemeroff CB. The state of our understanding of the pathophysiology and optimal treatment of depression: glass half full or half empty? *Am J Psychiatry*. 2020;177(8):671–685. https://doi.org/10.1176/appi.ajp.2020.20060845.
56. Belzung C, Willner P, Philippot P. Depression: from psychopathology to pathophysiology. *Curr Opin Neurobiol*. 2015;30:24–30. https://doi.org/10.1016/j.conb.2014.08.013.
57. Regiane Joca S, Araujo Moreira F, Wegener G. Atypical Neurotransmitters and the Neurobiology of Depression. *CNS amp Neurol Disord Drug Targets (Former Curr Drug Targets CNS amp Neurol Disord)*. 2015;14(8):1001–1011. https://doi.org/10.2174/1871527314666150909114804.
58. Black CN, Bot M, Scheffer PG, Cuijpers P, Penninx BWJH. Is depression associated with increased oxidative stress? A systematic review and meta-analysis. *Psychoneuroendocrinology*. 2015;51:164–175. https://doi.org/10.1016/j.psyneuen.2014.09.025.
59. D'Cruz M, Andrade C. Potential clinical applications of Ashwagandha (Withania somnifera) in medicine and neuropsychiatry. *Expert Rev Clin Pharmacol*. 2022;15(9):1067–1080. https://doi.org/10.1080/17512433.2022.2121699.
60. Zahiruddin S, Basist P, Parveen A, et al. Ashwagandha in brain disorders: a review of recent developments. *J Ethnopharmacol*. 2020;257, 112876. https://doi.org/10.1016/j.jep.2020.112876.
61. Speers AB, Cabey KA, Soumyanath A, Wright KM. Effects of Withania somnifera (Ashwagandha) on stress and the stress- related neuropsychiatric disorders anxiety, depression, and insomnia. 2021;19(9):1468–1495. https://doi.org/10.2174/1570159X19666210712151556.
62. Moncrieff J, Cooper RE, Stockmann T, Amendola S, Hengartner MP, Horowitz MA. The serotonin theory of depression: a systematic umbrella review of the evidence. *Mol Psychiatry*. 2023;28(8):3243–3256. https://doi.org/10.1038/s41380-022-01661-0.
63. Namdeo Mandlik DS. AG. Pharmacological evaluation of Ashwagandha highlighting its healthcare claims, safety, and toxicity aspects. *J Diet Suppl*. 2021;18(2):183–226. https://doi.org/10.1080/19390211.2020.1741484.