The efficacy and safety of St. John's wort extract in depression therapy compared to SSRIs in adults: A meta-analysis of randomized clinical trials

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Abstract

Background. Depression is the most common mental disorder, affecting about 3.8% of the population worldwide. Clinical symptoms of depression include sadness, anxiety and frequent mood swings, among others. Selective serotonin reuptake inhibitors (SSRIs), psychotherapy and behavioral therapy are commonly used for the treatment of this condition. Since SSRIs are associated with various side effects, extract of St. John's wort (SJW) has been suggested as an effective alternative. However, there are conflicting studies regarding its efficacy. Many studies have reported positive outcomes with low adverse effects, while others did not find it to be a suitable alternative.

Objectives. To analyze the available studies using SJW for depression therapy and to thoroughly evaluate its effectiveness compared to SSRIs and placebo.

Materials and methods. Relevant articles for our meta-analysis were found using Medline (via PubMed), Cinahl (via EBSCO), Scopus, and Web of Sciences databases. Studies were included as per the predefined Population, Intervention, Comparison, Outcomes and Study (PICOS) criteria. A demographic summary of the patients treated with either SJW, placebo or SSRIs was collected and Hamilton Depression Rating Scale (HAMD) scores were extracted. Risks of bias analysis, diagnostic odds ratio (OR), risk ratio (RR), and sensitivity calculation were evaluated using Revman software, and the publication bias was assessed using MedCalc software.

Results. Fourteen clinical trials with a total of 2270 depression patients were included in accordance with the inclusion criteria. All analyzed papers were published between 2000 and 2022. For patients treated with either SSRIs or SJW, a pooled OR of 2.44 with a 95% confidence interval (95% CI) of 1.33–4.45 was obtained. The data were heterogeneous, with a tau^2 value of 0.54, χ^2 value of 31.05, degrees of freedom (df) value of 7, I^2 value of 77%, and an overall Z-value of 2.90 with $p = 0.004$.

Conclusions. Our research supports the use of SJW as it reduced the number of depressive patients and their HAMD scores while having fewer risks and side effects than conventional medications.

Key words: mental disorder, SSRIs, depression, randomized controlled trials, St. John's wort

Introduction

Technology is developing day by day as is the lifestyle. To keep pace with the ongoing developments, people are involved in a lot of activities, which in turn causes anxiety, stress and various mental disorders. Currently, depression is the most common mental illness worldwide in people of all age groups. The clinical symptoms associated with depression are frequent mood swings, persistent sadness, anxiety, low appetite, irritation, sleeplessness, and loss of interest and pleasure in all activities, among others.[1,2] Major depressive disorders arise due to frontal lobe dysfunction out of threat and fear,[3,4] alterations in neuronal networks, and other cognitive impairments.[5–9] Medications, psychotherapy and behavioral therapy are the main treatment strategies for treating depression. The primary medicines used to treat depression are selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, paroxetine, sertraline, etc., as shown in Fig. 1, which outlines depression, its causes and medications used. Along with these, other drugs such as serotonin-noradrenaline reuptake inhibitor – noradrenaline and specific serotonergic antidepressants (SNRI–NaSSA) – can be used. However, these medications are associated with various adverse side effects like dizziness, indigestion, diarrhea, blurred vision, dry mouth, and others.[10,11] Therefore, for the effective treatment of depression with minimum side effects, various studies have reported the use of St. John's wort (SJW) extract.

Perforate SJW, also known as *Hypericum perforatum*, is a flowering plant from the Hyperaciae family; its extract is used as a herbal remedy for various mental illnesses like mild to moderate depression, obsessive-compulsive disorder, insomnia, etc. It is also an antioxidant with marked antiviral and antibacterial properties. St. John's wort is reported to reduce neuralgia, anxiety and stress by regulating neurotransmitters like serotonin, gamma-aminobutyric acid (GABA), dopamine, and others in the brain. Therefore, it has been used in the treatment of many neurological issues.

Various research articles and randomized controlled trials have reported SJW to effectively reduce the Hamilton Depression Rating Scale (HAMD) score and clinical symptoms in depressed patients.[12–25] For example, in a meta-analysis conducted by Linde and Mulrow, a total of 29 trials including 5489 patients were analyzed and the conclusion was that SJW is a safe medication for depression, superior when compared to existing SSRIs.[26] Similarly, Apaydin et al.,[27] Hübner and Kirste[28] and Behnke et al.[29] concluded that SJW used for depression is safe and more effective than placebo, with mild side effects.

However, the evidence regarding St. John's wort efficacy for the treatment of depression with fewer adverse effects is still insufficient since many studies, like the case study by Ferrara et al.[30] and Arold et al.,[31] did not find it perfectly safe and reported risk associated with its use in the treatment of depression. The contradictions regarding St. John's wort's safety and efficacy arise due to the limited amount of available case reports, use of unblinded assessments, and lack of refined analysis and evidence-level grade assessment. Therefore, the present study analyzes existing studies related to the use of SJW for depression, and summarizes the available literature in terms of efficacy and safety of SJW use to treat depression.

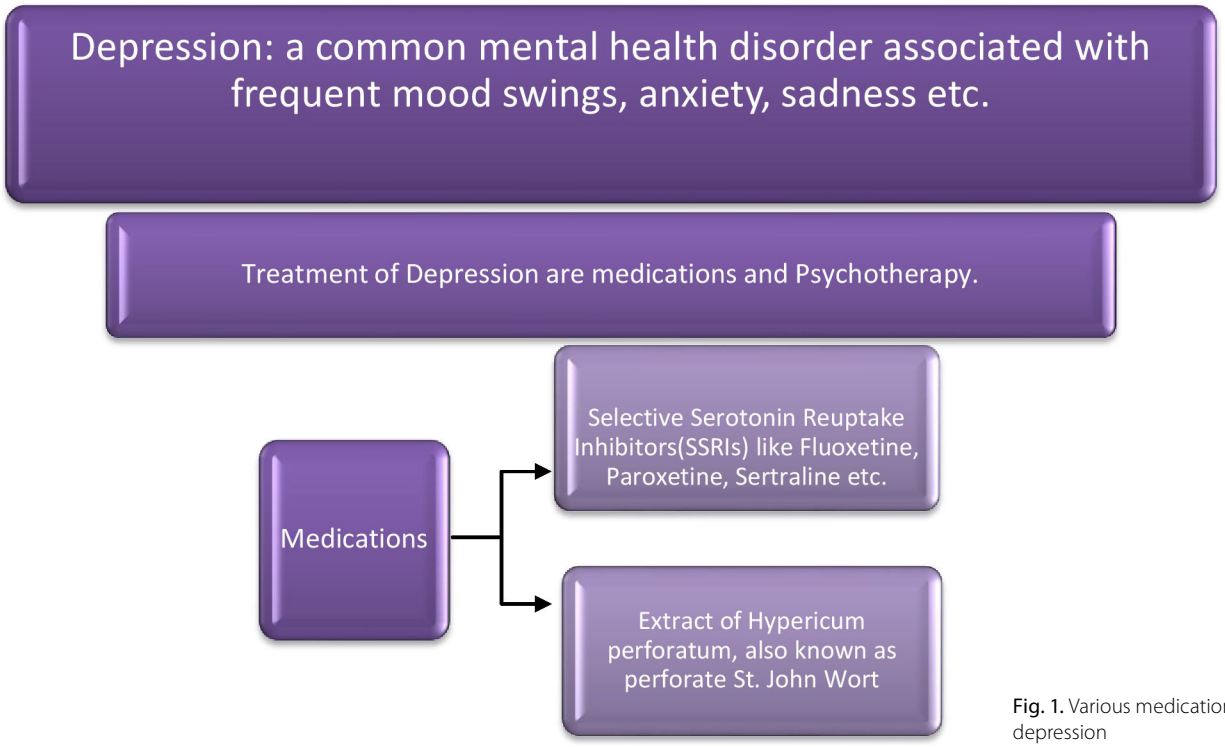


Fig. 1. Various medications used for depression

Objectives

The goal of this study was to analyze the efficacy of SJW extract in depression compared to SSRIs in adults.

Materials and methods

We followed the normative recommendations in the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) with a registration No. XU#/IRB/2021/1125.

Search strategy

This meta-analysis is based on an extensive search in Medline (via PubMed), Cinahl (via EBSCO), Scopus, and Web of Science databases for relevant studies published between 2000 and 2022. The following keywords were used to search for relevant studies: depression, neurological disorder, neurotransmitters, SSRIs, randomized controlled trials, anxiety, and HAMD score. All the included articles were selected as required by the PRISMA guidelines and studies were selected randomly irrespective of language, publication status or type of study (prospective, retrospective, clinical trial). A demographic summary of the patients and event data was extracted from the included studies.

Two authors (XZ and HZ) independently scanned the relevant sources for related studies. Mainly full-text articles were collected, and abstracts were used only if they included sufficient information for the meta-analysis. Obsolete references were excluded and valuable studies were included according to the inclusion criteria. In addition, 2 researchers (YW and CY) independently collected event data on useful variables.

Inclusion and exclusion criteria

We included studies that reported on the safety and efficacy of SJW in the treatment of adult patients with mild to moderate depression. Studies were selected from the year 2000 to 2022. Studies with insufficient data, reporting on the use of medications other than SSRIs and SJW, and published before 2000 were excluded.

Evaluation of the analytical standard

Two reviewers (XZ and HZ) independently evaluated the methodological validity of each included study and calculated the heterogeneity of the studies, while author CY was responsible for resolving any type of disagreement between XZ and HZ. To investigate the heterogeneity, a Deek's funnel plot, Cochran's Q statistic and I^2 index in random bivariate mode were calculated using RevMan software v. 5.0 (https://training.cochrane.org/online-learning/core-software/revman/).

Sources of heterogeneity and risk of bias assessment

The heterogeneity sources investigated included the use of full-text publications compared to abstracts, varied age groups, different numbers of patients, variable durations of treatment, different scales of analysis, and comparison of SJW to placebo and different SSRI medicines.

The risk of bias assessment for the included studies was performed, and the corresponding risk of bias summary and graph were created using RevMan v. 5.0.[32]

Statistical analyses

The meta-analysis was performed using extracted data, and statistical parameters such as diagnostic odds ratios (ORs), relative risks with a 95% confidence interval (95% CI), and sensitivities were calculated using the Mantel–Haenszel method with random bivariate effects using RevMan v. 5.0, along with their respective forest plots.[33] Meta-analyses were performed using a random-effects model (Mantel–Haenszel method), and the heterogeneity of the included studies was evaluated using a tau^2 value, χ^2 value, I^2 value, and Z-value. A value of $p < 0.05$ was considered statistically significant. Diagnostic ORs were calculated using the DerSimonian–Laird technique. For this, a 2×2 table was made and a meta-analysis was performed using RevMan software v. 5.0. A pooled diagnostic OR with a 95% CI was calculated and respective forest plots were created. The publication bias of the included studies was assessed using Begg's and Egger's tests,[34] and a funnel plot was prepared by plotting the log risk ratio (RR) of each study against its standard error using MedCalc software v. 20.115 (MedCalc Software Ltd., Ostend, Belgium).

Results

Literature search results

We found a total of 1135 studies through electronic searches of different databases. We excluded 148 studies after reading their titles and abstracts, leaving 987 records to be screened. Furthermore, due to invalid references and duplications, we excluded 881 studies, and included only 106 studies for the final screening. Out of these, 75 studies were excluded based on our inclusion criteria, and the eligibility of the remaining 31 was further assessed. The key reasons for exclusion included inadequate evidence and comparison criteria inappropriate to create 2×2 tables for review. The 14 studies that fulfilled the inclusion criteria (i.e., the use of SJW compared to SSRI) and were chosen for this meta-analysis are shown in Fig. 2.

The demographic details of the included studies are shown in Table 1. They include the author of the study, year of publication, duration of the study, total sample size,

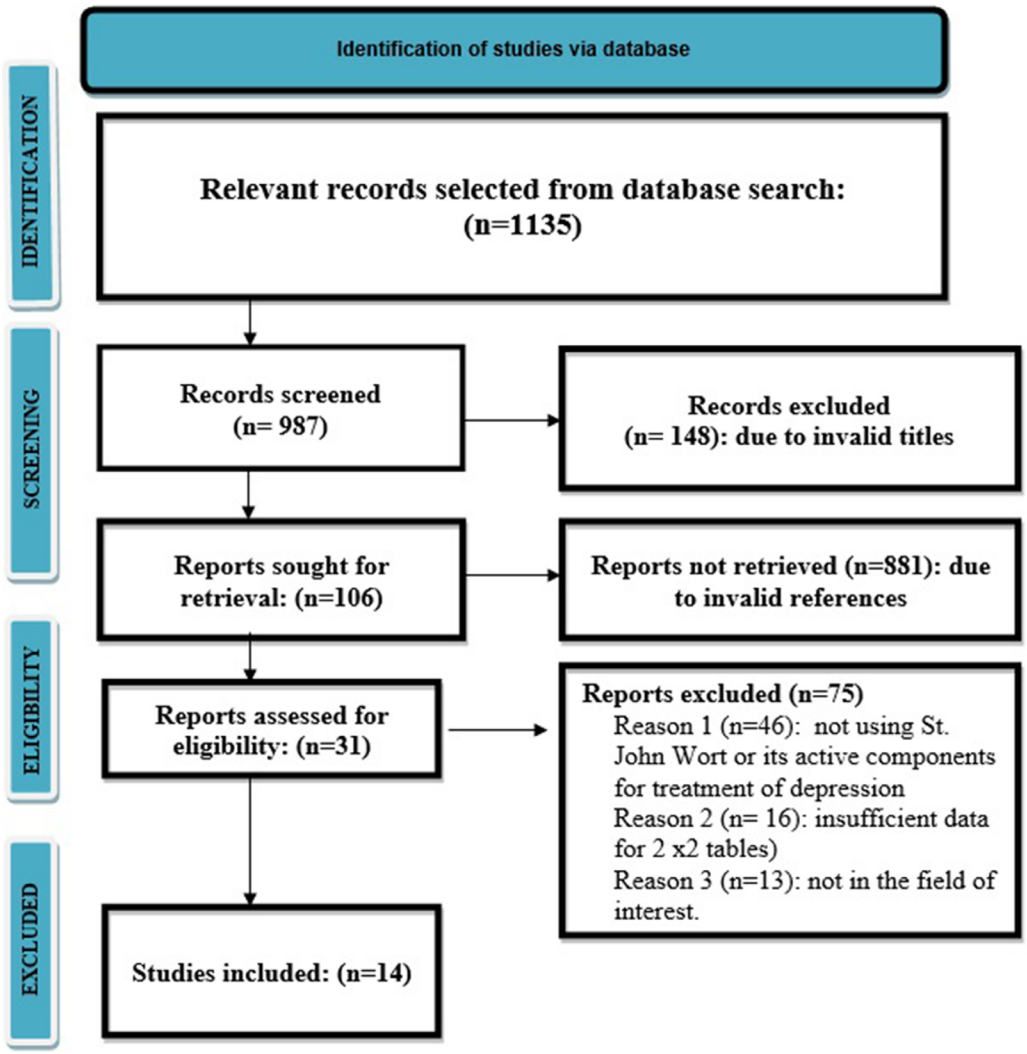


Fig. 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram of the study group

type of SSRI drug used as the control, dose of the drugs used, age and gender of the patients, number of patients with positive outcomes, the initial HAMD score of patients, and the mean value and standard deviation (M ±SD) of improved HAMD scores, with their respective p-values for statistical significance.

Fourteen clinical trials with a total of 2270 patients suffering from depression were included according to the inclusion criteria. The included studies evaluated adult patients from different age groups who were randomly chosen and treated with either a conventional SSRI like fluoxetine and sertraline, or placebo, and SJW. In both cases, the number of patients with a reduction in their HAMD scores and a marked improvement in clinical symptoms were extracted as event data and analyzed statistically.

Risk of bias assessment

The risk of bias assessment for the included studies is reported in Table 2. The risk of bias was low as evident from the corresponding risk of bias summary shown in Fig. 3 and the risk of bias graph presented as Fig. 4.

Meta-analysis results

Results for improvement in HAMD score of patients using either SJW or placebo

The risk of publication bias in the included studies related to the treatment with either SJW or placebo was low, as shown in the funnel plot in Fig. 5. We obtained the value of $p = 0.85$ for Begg's test and $p = 0.68$ for Egger's test, which confirms a low risk of publication bias.

We calculated a pooled OR of 0.72 with a 95% CI of 0.64–0.81, as shown in the forest plot in Fig. 6. The data were heterogeneous with a tau^2 value of 0.36, a χ^2 value of 17.93, a degrees of freedom (df) value of 5, an I^2 value of 72%, and an overall Z-value of 2.60 with $p = 0.009$. We obtained a pooled RR of 0.46 with a 95% CI of 0.26–0.83, as shown in the forest plot in Fig. 7. The data were heterogeneous, with a χ^2 value of 5.34, df value of 5, and an overall Z-value of 5.36 with $p = 0.00001$. All of these results were statistically significant with $p < 0.05$.

Table 1. Demographic summary of the included studies

Study and year	Sample size, n	Age [years]	Gender (F/M)	Duration [weeks]	Control drug			Test drug (SJW)		
					dose	positive response in patients with test drug	p-value	SJW extract dose	positive response in patients with control drugs	p-value
Hypericum depression trial study group 2002 [12]	340 mean HAMD ≥20	above 18 years	147/77	8	sertraline 50–100 mg/day	n = 79/111 M ±SD = 10.53 ±0.72	p = 0.21	900–1500 mg	n = 82/113 M ±SD = 8.68 ±68	p = 0.26
Lecrubier et al. 2002 [17]	375 mean HAMD ≥ 25	18–65	287/88	6	placebo	n = 80/189 M ±SD = 8.5 ±7.7	p = 0.04	300 mg/day	n = 98/189 M ±SD = 10.5 ±7	p = 0.237
Van Gurp et al. 2002 [14]	87 mean HAMD ≥ 16	18–65	52/33	12	sertraline 50–100 mg/day	n = 28/43 M ±SD = 11.5 ±8.4	p = 0.237	900–1800 mg/day	n = 30/43 M ±SD = 9.4 ±8.3	p = 0.237
Moreno et al. 2005 [18]	53 mean HAMD ≥ 20	19–64	44/9	8	fluoxetine 20 mg/day	n = 3/16 mean HAMD ≤ 10	p = 0.3794	900 mg/day	n = 6/18 mean HAMD ≤ 10	p = 0.0167
Fava et al. 2005 [13]	135 mean HAMD = 19.7 ±3.2	18–65	77/58	12	placebo 20 mg/day	n = 9/43 M ±SD = 12.6 ±6.4	p = 0.096	900 mg/day	n = 17/43 M ±SD = 10.2 ±6.6	p < 0.03
Bjerkenstedt et al. 2005 [12]	163 mean HAMD = 30	18–70	129/34	6	placebo 20 mg/day	n = 21/55 M ±SD = 15 ±8.4	p = 0.7	900 mg/day	n = 22/55 M ±SD = 15.5 ±6.7	p = 0.7
Szegedi et al. 2005 [24]	251 mean HAMD = 22	20–60	168/83	6	paroxetine 20 mg	n = 73/125 M ±SD = 11.4 ±8.6	p = 0.01	900 mg/day	n = 86/125 M ±SD = 14.4 ±8.8	p = 0.01
Simeon et al. 2005 [22]	26 mean HAMD = 18	12–17	14/12	8	sertraline 50 mg/day	n = 5/26 M ± SD = 10.8 ±5.3	p = 0.016	900 mg/day	n = 21/26 M ±SD = 10.8 ±5.3	p = 0.016
Kasper et al. 2006 [16]	332 mean HAMD = 18	18–65	205/127	6	placebo	n = 74/119 M ±SD = 17.6 ±8.8	p < 0.001	600 mg/day	n = 111/119 M ±SD = 11.8 ±8.3	p < 0.001
Ur-Rahman et al. 2008 [19]	112 mean HAMD = 18	18–65	87/25	6	placebo 300 mg thrice daily	n = 23/56 M ±SD = 10.04 ±0.8	p = 0.4	300 mg thrice daily	n = 35/56 M ±SD = 8.04 ±1.0	p = 0.4
Weber et al. 2008 [25]	54 mean HAMD = 18	6–17	20/34	8	placebo	n = 12/27 mean HAMD ≤ 10	p = 0.89	300 mg/day	n = 14/27 mean HAMD ≤ 10	p = 0.68
Singer et al. 2011 [23]	154 mean HAMD ≥ 20	18–74	73/35	6	20 mg citalopram	n = 24/54 mean HAMD ≤10	p = 0.0288	900 mg/day	n = 26/54 mean HAMD ≤ 10	p = 0.0288
Sarris et al. 2012 [20]	124 mean HAMD = 18	18–60	81/43	26	sertraline 50–100 mg/day	n = 64/124 M ±SD= 7.1 ±5.4	p = 0.036	900–1500 mg/day	n = 105/124 M ±SD = 6.6 ±4.5	p = 0.03
Seifritz et al. 2016 [21]	64 mean HAMD = 25	18–70	31/32	6	paroxetine 20 mg/day	n = 8/33 M ±SD = 22.9 ±0.8	p = 0.248	3 × 300 mg/day	n = 20/31 M ±SD = 23.1 ±0.9	p = 0.248

SJW – St. John's wort; HAMD – Hamilton Depression Rating Scale; M ±SD – mean value ± standard deviation.

Table 2. Risk assessment for included studies

Question	Bjerkenstedt et al. 2005 [12]	Fava et al. 2005 [13]	Van Gurp et al. 2002 [14]	Hypericum Depression Trial (HTD) group 2002 [15]	Kasper et al. 2006 [16]	Lecrubier et al. 2002 [17]	Moreno et al. 2005 [18]	Ur-Rahman et al. 2008 [19]	Sarris et al. 2012 [20]	Seifritz et al. 2016 [21]	Simeon et al. 2005 [22]	Singer et al. 2011 [23]	Szegedi et al. 2005 [24]	Weber et al. 2008 [25]
Was a consecutive or random sample of patients enrolled?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did the study avoid inappropriate exclusions?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did all patients receive the same reference standard?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were all patients included in the analysis?	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Was the sample frame appropriate to address the target population?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were study participants sampled in an appropriate way?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the study subjects and the setting described in detail?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were valid methods used for the identification of the condition?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the condition measured in a standard, reliable way for all participants?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was there appropriate statistical analysis?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

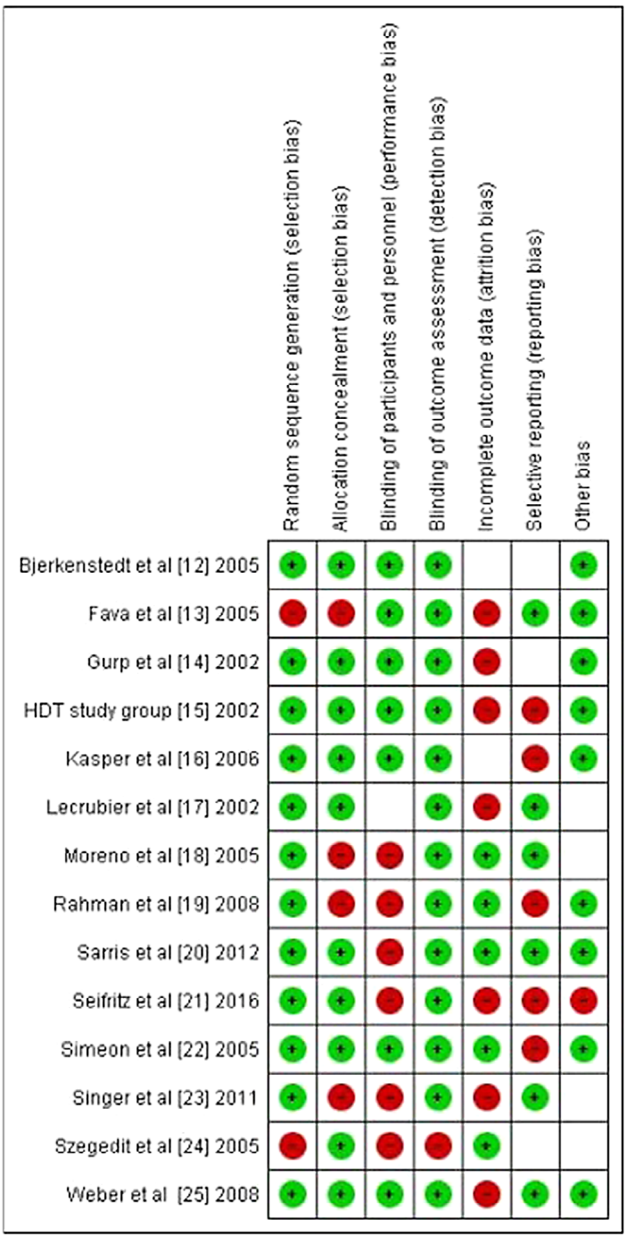


Fig. 3. Risk of bias summary

Results for improvements in HAMD scores of patients using either SJW or SSRIs

The risk of publication bias in the included studies related to the treatment with either SJW or SSRIs was low, as shown in the funnel plot in Fig. 8. We obtained the value of p = 0.80 for Begg's test and p = 0.76 for Egger's test, which confirms a low risk of publication bias.

We calculated a pooled OR of 2.44 with a 95% CI of 1.33–4.45, as shown in the forest plot in Fig. 9. The data were heterogeneous, with a tau^2 value of 0.54, a χ^2 value of 31.05, a df value of 7, an I^2 value of 77%, and an overall Z-value of 2.90 with p = 0.004. We obtained a pooled RR of 1.39 with a 95% CI of 1.09–1.76, as shown in the forest plot in Fig. 10. The data were heterogeneous with a tau^2 value of 0.07, a χ^2 value of 31.43, a df value of 7, an I^2 value of 78%,

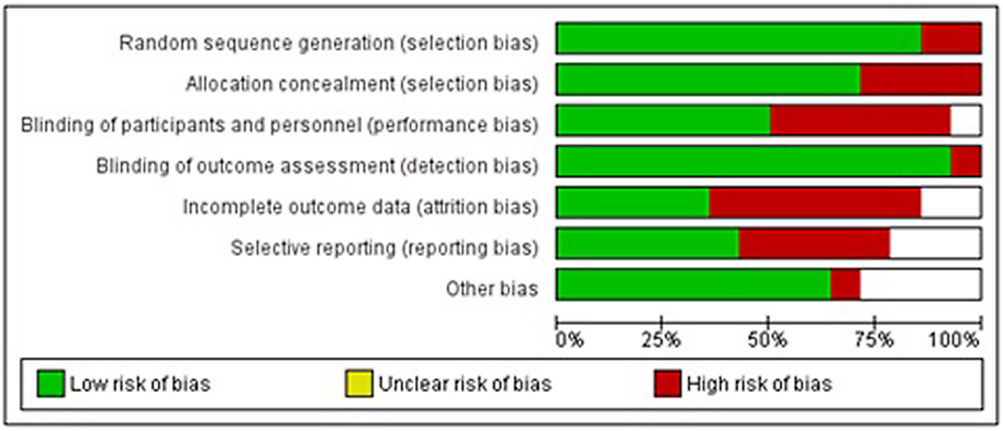
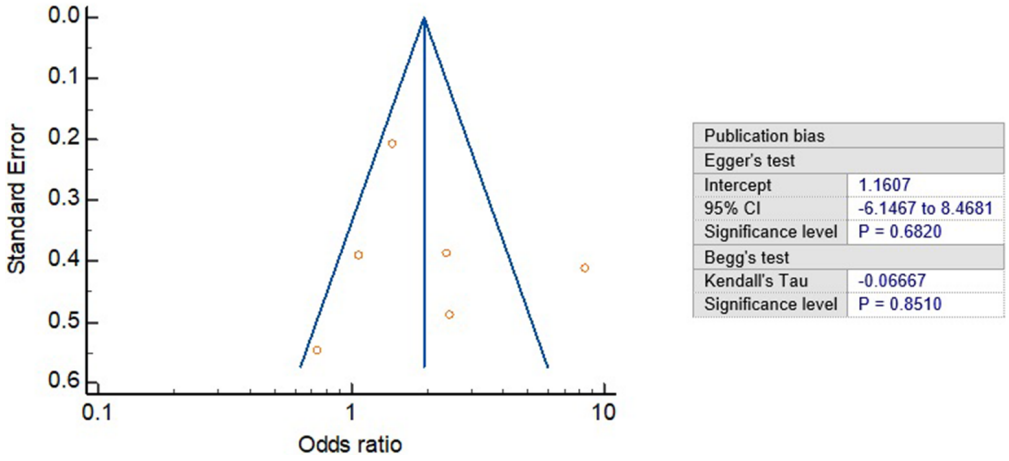


Fig. 4. Risk of bias graph



Publication bias	
Egger's test	
Intercept	1.1607
95% CI	-6.1467 to 8.4681
Significance level	P = 0.6820
Begg's test	
Kendall's Tau	-0.06667
Significance level	P = 0.8510

Fig. 5. Funnel plot of St. John's wort (SJW) compared to placebo

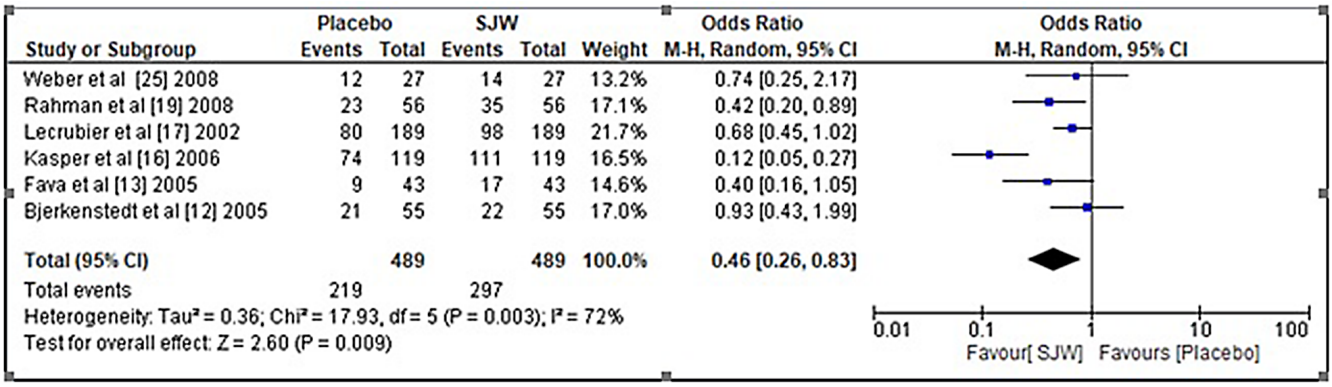


Fig. 6. Forest plot of odds ratio (OR) of St. John's wort (SJW) compared to placebo

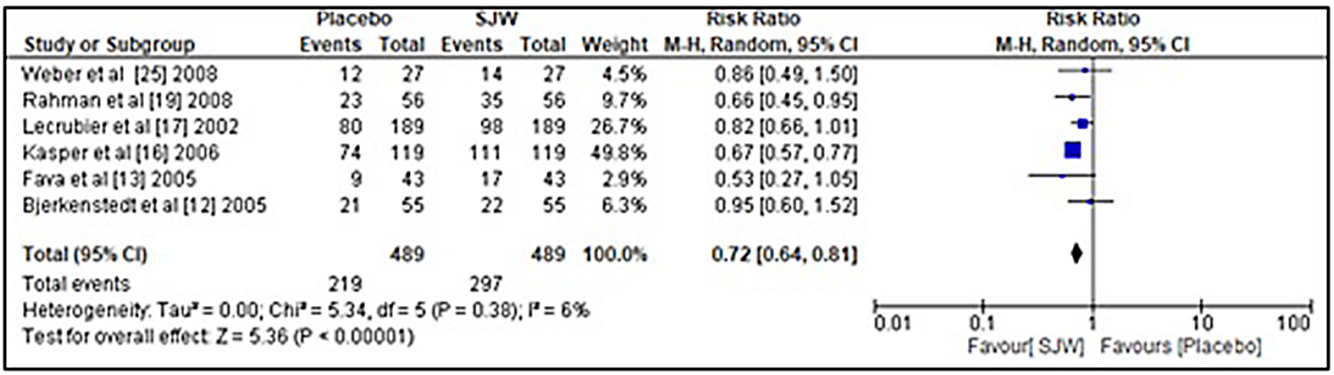


Fig. 7. Forest plot of risk ratio (RR) of St. John's wort (SJW) compared to placebo

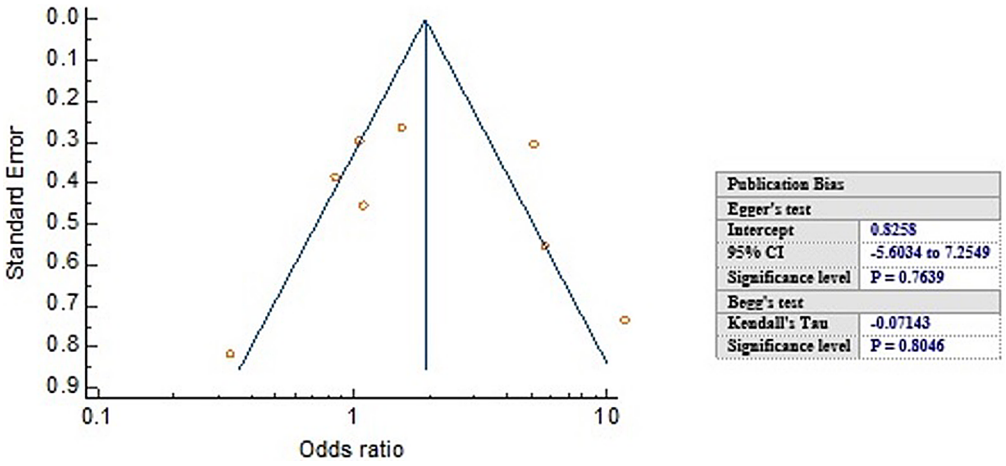


Fig. 8. Funnel plot of St. John's wort (SJW) compared to selective serotonin reuptake inhibitors (SSRIs)

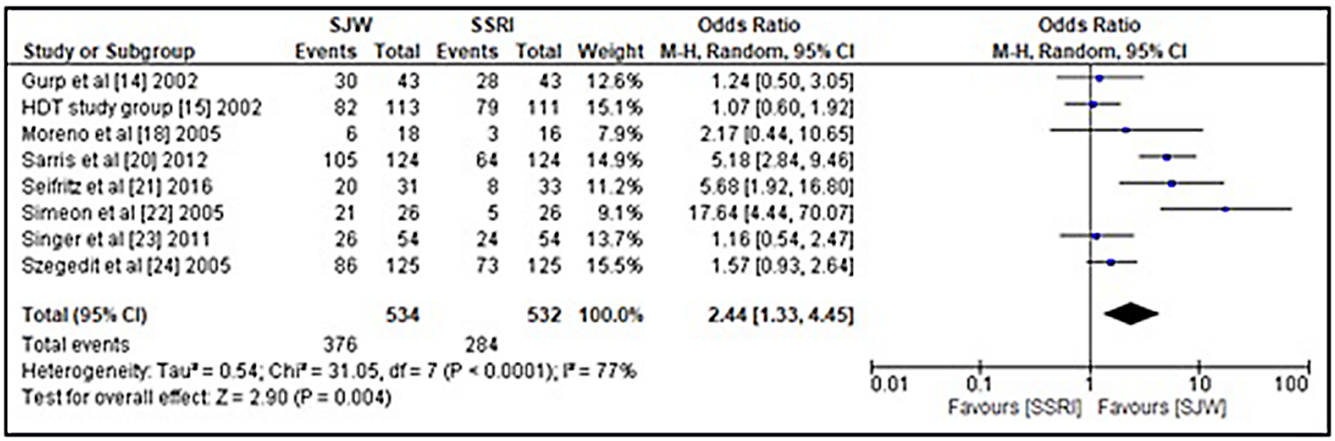


Fig. 9. Forest plot of odds ratio (OR) of St. John's wort (SJW) compared to selective serotonin reuptake inhibitors (SSRIs)

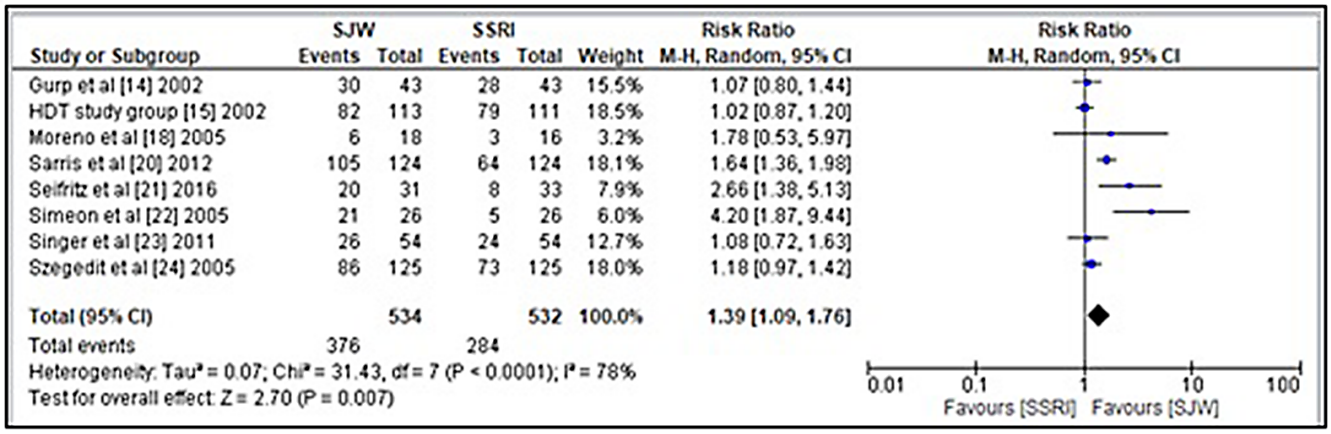


Fig. 10. Forest plot of risk ratio (RR) of St. John's wort (SJW) compared to selective serotonin reuptake inhibitors (SSRIs)

and an overall Z-value of 2.70 with p = 0.007. All of these results were statistically significant with $p < 0.05$.

The statistical data are summarized in Table 3 and these results showed SJW to be more effective than placebo and conventional SSRIs, with statistically significant sensitivity of 80%. A greater number of patients with reduced HAMD scores was observed in both comparisons of SJW to placebo and SJW to SSRIs. This proves that SJW is a more effective and better alternative for the treatment of depression. Considering all of these statistically significant results with $p < 0.05$, this study supports the use of SJW in adults with mild to moderate depression.

Discussion

Depression is a mental disorder that arises from a hectic and stressful lifestyle. When a person finds themselves

Table 3. Statistical summary of the included studies

Study, year, reference	OR (95% CI)	RR (95% CI)	Sensitivity (%)
Lecrubier et al., 2002 [17]	0.68 (0.45–1.02)	0.82 (0.66–1.01)	84.5
Van Gurp et al., 2002 [14]	1.24 (0.50–3.05)	1.07 (0.80–1.44)	93.8
Hypericum Depression Trial (HTD) group 2002 [15]	1.07 (0.60–1.92)	1.02 (0.87–1.20)	96.5
Simeon et al., 2005 [22]	17.64 (4.44–70.07)	4.20 (1.87–9.44)	56.8
Moreno et al., 2005 [18]	2.17 (0.44–10.65)	1.78 (0.53–5.97)	66.7
Fava et al., 2005 [13]	0.40 (0.16–1.05)	0.53 (0.27–1.05)	68.0
Bjerkenstedt et al., 2005 [12]	0.93 (0.43–1.99)	0.95 (0.60–1.52)	95.7
Szegedi et al., 2005 [24]	1.57 (0.93–2.64)	1.18 (0.97–1.42)	92.5
Kasper et al., 2006 [16]	0.12 (0.05–0.27)	0.67 (0.57–0.77)	75.0
Weber et al., 2008 [25]	0.74 (0.25–2.17)	0.86 (0.49–1.50)	87.5
Ur-Rahman et al., 2008 [19]	0.42 (0.20–0.89)	0.66 (0.45–0.95)	74.5
Singer et al., 2011 [23]	1.16 (0.54–2.47)	1.08 (0.72–1.63)	92.9
Sarris et al., 2012 [20]	5.18 (2.84–9.46)	1.64 (1.36–1.98)	71.9
Seifritz et al., 2016 [21]	5.68 (1.92–16.80)	2.66 (1.38–5.13)	62.5

OR – odds ratio; 95% CI – 95% confidence interval; RR – risk ratio.

lagging behind others, their mental well-being becomes disturbed and they persistently remain sad and stressed.[35,36] Depression has a significant impact on a patient's social behavior and results in people separating themselves from society and indulging in bizarre thinking. If the problem escalates, it can lead to borderline personality disorder as well contemplating self-harm and suicide.[37–40]

For the treatment of mild to moderate depression, self-care and psychological therapies are initially suggested. If the condition of the patient does not improve, medications may be used. For this purpose, SSRIs like fluoxetine, paroxetine and sertraline are generally used, but their utility is limited by their adverse side effects such as dizziness, indigestion and diarrhea.[41–45] Therefore, to achieve an effective treatment of depression with minimum side effects, various studies reported the use of SJW extract, which is a well-known herbal remedy for various mental illnesses. It selectively regulates neurotransmitters in the brain and is useful in the treatment of neurological issues.

Various studies, including Fava et al.,[13] Van Gurp et al.,[14] Moreno et al.,[18] and Singer et al.,[23] reported that SJW can effectively reduce HAMD scores and clinical symptoms of depression. Linde and Mulrow performed a meta-analysis that included a total of 29 studies with 5489 patients, and concluded that SJW is equally safe in depression patients as compared to existing SSRIs, and superior to SSRIs in terms of safety and minimal adverse effects. Similarly, Apaydin et al.[27] evaluated 35 studies that included 6993 patients for the efficacy of SJW, Behnke et al.[29] performed a double-blind randomized controlled trial with SJW, and Hübner and Kirste[28] studied the effect of SJW in 101 children under 12 years of age. All found SJW to be a safer and more effective medicine than placebo, with mild side effects. Similarly to these studies, we also found a pooled OR of 2.44 with a 95% CI of 1.33–4.45 for SSRIs compared to SJW, and a pooled OR of 0.46 with a 95% CI of 0.26–0.83 for placebo compared to SJW. With these statistically significant ($p < 0.05$) results and a statistically significant sensitivity of 80%, we recommend SJW as an efficient drug for adults with mild to moderate depression.

Unlike our results, case studies by Ferrara et al.[30] and Arold et al.[31] did not find SJW to be a perfectly safe and convincing alternative. They reported risks associated with its use, and suggested checking its dose and side effects more carefully before using it in the treatment of depression. Recent studies have reported that if depression occurs because of changes in neuronal networks or alterations in brain complexes, non-invasive brain surgery is a good treatment option instead of medications.[46–50] Battaglia et al. also reported that understanding the psychophysiology of fear can help in finding new insights for the characterization of mental illnesses.[51]

Limitations

The limitation of the present study is the variability of control drugs used for the treatment of depression compared to SJW, which could have skewed our results. Similarly, the observation of HAMD score and clinical symptoms using different analytical tests performed by different persons also influences the risk of false negative results. Many studies failing to report on the comparable efficiency of SJW with conventional SSRI drugs may also affect the data to some extent. Data from other relevant studies showing the efficacy of SJW compared to SSRIs could have included more results to suggest its use more precisely. Detailed data from the patient's case history, physical examination and pathological tests can further improve the results supporting SJW as an effective treatment for mild to moderate depression.

Conclusions

The SSRIs are widely used for the treatment of depression and can significantly alleviate clinical symptoms and lower the HAMD score. However, due to their strong side effects, they are not recommended. Instead, the use of SJW is preferred as it is a cheap, readily available and effective treatment strategy for mild to moderate depression, with mild side effects. Thus, based on the current meta-analysis and statistically significant results ($p < 0.05$), the use of SJW for depression in adults is strongly recommended.

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