

## Treatment of Depression, Anxiety, and Sleep disorders by Homeopathic Medicines: A Systematic Review

Atif Raza (1, 2, 3), Sajjad Ali (1, 2), Muhammad Zubair Qureshi (1), Iqra Saleem (4), Asia Raza (1), Sehrish Rasheed (1), Mubeen Ashraf (1), Farhat Yasmeen (1)

(1) Pakistan Homeopathic College, Hospital and Research Center, Lahore, Pakistan

(2) Rashid Latif College of Pharmacy, Lahore, Pakistan

(3) University College of Pharmacy, University of the Punjab, Lahore, Pakistan

(4) The University of Poonch, Rawalakot, Azad Kashmir

### ABSTRACT

**Background:** Depression is a serious health issue and a disease, which is affecting a large number of people around the world. It is disturbing the whole cosmos of life. The purpose of this systematic review was to evaluate the effectiveness of homeopathic medicines for the treatment of depression, anxiety and sleep disorders.

**Methodology:** A computerized comprehensive research was carried to find out clinical research articles related to depression, anxiety and sleep disorders. For this purpose, Pub med, Google scholar, Sci-Hub, Medline, Science direct and Thieme-E-journal of Homeopathy were searched extensively. Only full length articles were included. Articles with only abstract, animal trials, case studies were excluded. Only human based trials were included. All randomized double-blind placebo controlled prospective observational open label studies were included.

**Results:** Total 60 articles were studied. Duplicate and irrelevant articles were removed. 22 full length articles were included in this systematic review. All articles were dealing with the different forms of depression by homeopathic medicines.

**Conclusion:** This systematic review concluded that homeopathic medicines are safe and effective in the treatment of different forms of depression and anxiety. However, there is a need for more randomized placebo controlled clinical trials to strengthen the results, and in that duration of homeopathic treatment should be somewhat longer to get better results. In the future, there should be research on depression with insomnia that is a very common symptom of depression.

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### INTRODUCTION

Depression is a common mental health problem which is presented by depressed mood, anxiety, disturbed sleep, eating disorders, low self esteem, low energy, lack of interest in all activities and pleasures of life, desperation and intense feeling of sadness (1, 2). World wide it is a major mental health issue (3). Sleep, anxiety or depressive disorders are the common mental health issues due to which quality of life affects badly (4). Depressive disorders are very common in primary care

but a significant number of patients develop chronic illnesses despite this fact that many patients have good outcomes in the short term (5).

Globally, major depressive disorder is the fourth most disabling condition and in the year 2020, it is expected to be ranked second. Women are twice prone to depression than men (6) Depression is the leading cause of disability while it affects 121 million people worldwide (7, 8) and less than 25% have access adequate treatment (8-10). Patients are not satisfied with the use of antidepressant

as it has several adverse effects that is why they choose other treatment options (11-13) Depression is the main reason of using alternative and complementary medicine (9) because there are a significant number of patients who prefer homeopathy as a way of treatment for depressive disorders (14, 15).

Homeopathic mode of treatment is based on taking case history and selection of individualized medicine according to the patient's individuality (15). Homeopathy is based on the principle of 'likes with likes' means the substance which can produce symptoms in a healthy individual is also capable of treating the same symptom when he is ill by using it in highly diluted forms (3, 9). In homeopathy totality of symptoms is considered important with patient's individuality for selection of good medicine (9). This is the reason that most patients with anxiety and depression like to consult homeopaths (16). Depression is the most frequently treated complaint in the outpatient department of homeopathic hospitals and UK National Health Services (9). Thus, the purpose of this systematic review was to evaluate the effectiveness of homeopathic medicines for the treatment of depression, anxiety and sleep disorders.

## METHODOLOGY

A computerized comprehensive was searched to find out clinical research articles related to depression. For this purpose, Pub med, Google scholar, Sci-Hub, Medline, Science direct and Thieme-E-journal of Homeopathy were searched extensively. In this review, only human based clinical trials were included. However, animal trials, case studies, and pilot studies were not included. Only full-length research articles were included. All randomized double blind placebo controlled, prospective observational clinical research articles were included. We have excluded articles, which were not related to our research topic. Opinion papers were also not included in this review.

Total 60 articles were searched from a different database, out of which eight were excluded due to irrelevance of topic. Reviewer has reviewed the articles independently. Total 30 articles were excluded due to exclusion criteria and only 22 articles were according to our inclusion

criteria as shown in figure 1.

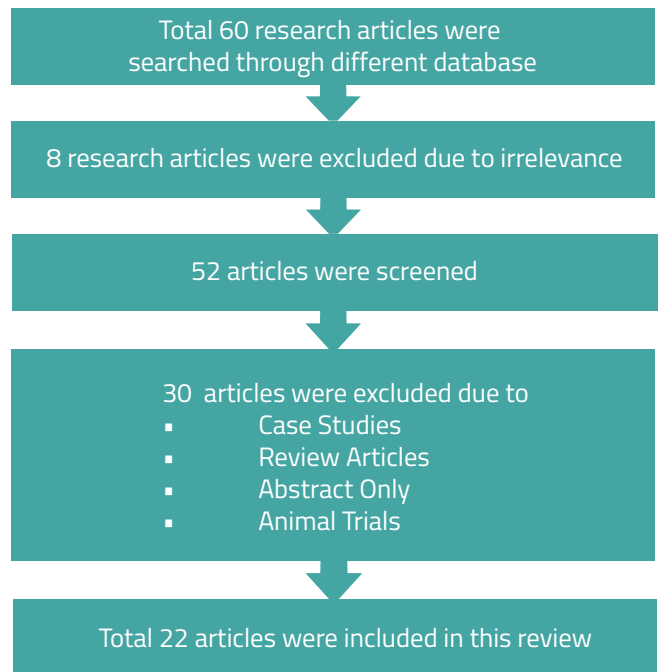


Figure 1: Overview of study

## RESULTS

Total 22 full-length articles were included in this review as shown in below tables. A Cohort of multiple randomized controlled trials was conducted by Viksveen and the major findings of this article were that use of homeopathic medicines against self care treatment is much better and effective (3). Another clinical trial concluded that Homeopathic medicine *Hypericum Perforatum* was not effective in the treatment of moderately severe depression (17). Uberitan designed a prospective double blind, double-dummy trial of homeopathic Q potencies versus Fluoxetine. This trial concluded that there is no inferiority of homeopathic medicines to Fluoxetine group (18).

Another study of Grimaldi-Bensouda the EPI3 Cohort studies showed that for anxiety and depression issues homeopathic medicines are far better than generally used conventional medicines. The patient using homeopathic medicines had less use of psychotropic drugs than non homeopathic users (19). Ubertin C Adler concluded that results of homeopathic Q potencies

versus conventional and placebo are not conclusive due to certain limitations (15). An open label observational study was conducted by Oberai. Major findings of this study was that homeopathic treatment is very beneficial for depressive episodes (16). However, Moreno study's major findings were that homeopathic medicine *Hypericum perforatum* was less efficacious than

*fluoxetine* and placebo. This randomized double blind clinical trial was conducted in patients with moderate to severe depression (20).

A randomized double-blind control trial was conducted in which *Hypericum perforatum* versus *Fluoxetine* was used in the treatment of mild to moderate depression. The *Hypericum* preparation tested in this study is

Paper Ref	Drug	Pat. No	Disease	Research Methodology	Major Findings
Viksveen et al., 2017 (3)	Homeopathic medicines	566	Depression	Cohort multiple randomized controlled trial	This trial provides preliminary support for both the acceptability and the effectiveness of treatment by a homeopath for patients with self-reported depression.
Group, 2002 (17)	<i>Hypericum perforatum</i>	340	Moderately severe major Depression	Double-blind, Randomized, Placebo-controlled trial	<i>Hypericum</i> fail to support the evidence that it is effective in moderate to severe major depression.
Uberitan et al., 2011 (18)	Individualized Q-Potencies Vs Fluoxetine Clonazepam diazepam	91	Moderate to severe Depression	Prospective, randomized, double-blind, double-dummy trial,	Study shows non-inferiority of Homeopathic Q potencies as compared to Fluoxetine in acute treatment of outpatient with moderate to severe depression.
Grimaldi-Bensouda et al., 2016 (19)	Homeopathic medicines	710	Anxiety and depression disorder	The EPI3 Cohort studies	Patients with ADD, who chose to consult GPs prescribing homeopathy reported less use of psychotropic drugs, and were marginally more likely to experience clinical improvement, than patients managed with conventional care.
Ubiratan C Adler et al., 2013 (15)	Homeopathic Q potencies placebo	44	Mild to moderate Depression	Randomized, partially double-blind, placebo-controlled, four-armed trial	Results are inconclusive, given that recruitment into this trial was very difficult and we had to terminate early.
Oberai et al., 2013 (16)	Natrum muriaticum, Arsenic Album, Pulsatilla, Lycopodium and Phosphorus	83	Depressive episodes	Prospective, non-comparative, open label observational study	A course of six months of homeopathic treatment is associated with significant benefits in patients suffering from depressive episodes, as measured by HDRS.
Moreno et al., 2006 (20)	<i>Hypericum perforatum</i> 900 mg/day Vs. Fluoxetine 20mg/day and placebo	72	Mild to moderate depression	Randomized double-blind trial in a Brazilian sample	<i>Hypericum perforatum</i> was less efficacious than both Fluoxetine and placebo. Both drugs were safe and well-tolerated.

Behnk et al., 2002 (21)	Hypericum perforatum Vs. Fluoxetine hydrochloride	70	Mild to moderate depression	Randomized, controlled, double-blind trial	The Hypericum preparation tested in this study is therapeutically equivalent to Fluoxetine and is therefore a rational alternative to synthetic antidepressants
C. E. Macías-Cortés et al., 2015 (22)	Individualized homeopathic medicine Vs. Fluoxetine Vs. Placebo	133	Moderate to severe depression	A randomized, placebo-controlled, double-blind, double-dummy, superiority, three-arm trial	Homeopathy and Fluoxetine are effective and safe anti-depressants for climacteric women. Homeopathy and Fluoxetine were significantly different from placebo in response definition Only
Bagherian et al., 2014 (23)	Individualized homeopathic medicines in 30 C Vs. Placebo	30	Symptoms of anxiety and depression	Randomized, Double Blind and Placebo Controlled	Findings suggest that homeopathic therapy can be used as an effective method to treat anxiety and depression disorders

**Table 1: Clinical Trials Related To Depression**

therapeutically equivalent to Fluoxetine and is, therefore, a rational alternative to synthetic anti-depressants (21). A randomized, placebo-controlled, double blind, double dummy, superiority, and three-arm trial was conducted by C. E. Macías-Cortés. This study concluded that Homeopathy and Fluoxetine are effective and safe anti-depressants for women at climacteric age (22). Bagherian designed a randomized double-blind placebo controlled trial. Its major findings were that homeopathic individualized medicines in 30 C are very good in controlling symptoms of anxiety and depression (23). Major findings of a comparative study were that hypericum perforatum and passion flower both have very good effects in the treatment of depression, insomnia and anger at menopausal age (24). Another study revealed that that passion flower (passiflora) is effective as add on treatment with sertraline in the treatment of generalized anxiety with low side effects (24). While a double-blind placebo-controlled trial showed that passiflora in single and multiple doses is effective in controlling human stress and heart signals (25). Hubner designed a prospective, non-randomized, non interventional, observational study. Main findings of this study were that homeopathic preparation "Neurexan" works better than combination formulations based on valerian extracts in nervousness and restlessness (26).

While Takara randomized, placebo-controlled, double-blind trial showed that passion flower (passiflora) extract is effective in improving anxiety (27). Halder conducted a randomized double-blind placebo-controlled trial. In this trial, homeopathic individualized C-potencies, Fluoxetine and placebo were used for the treatment of anxiety and depression. Results of the trial were inconclusive due to certain reasons (28).

A double-blind placebo-controlled trial was conducted by Movafegh and results showed that passiflora Incarnata is very effective in treating pre-operative surgery anxiety without giving any sedatives to the patients (29). Major findings of a single blind clinical trial was that chamomile tea is very effective in treating anxiety and depression of cancer patients (30). While major findings of a prospective study designed by Biswas were that homeopathic medicines were effective in the treatment of depression with suicidal tendency when chosen carefully according to the individuality of the patient (31). Villet designed an open-label observational study. This study showed that passiflora composition could be used effectively. For the treatment of anxiety and sleep disorder and it can be used as an alternative to psychotropic drugs (32).

A randomized placebo-controlled clinical trial was

conducted by Katz for depression with fluxetine and homeopathic drugs and major findings were not feasible due to recruitment difficulties and patient's preferences (33). While Bonne showed in double blind placebo-controlled study that effects of homeopathic remedies and placebo for mental symptoms are the

same, they do not differ much from one another. As results of both categories were substantial (34).

## DISCUSSION

This systematic review was carried out to establish the fact that homeopathic medicines are effective in the

Paper Ref	Drug	Pat. No	Disease	Research Methodology	Major Findings
Fahami et al., 2010 (24)	Hypericum perforatum vs. Passion flower (passiflora)	59 Women	Depression Insomnia Anger	Comparative study	Hypericum Perforatum and Passion Flower (passiflora) on treating menopause precocious symptoms (vasomotor signs, insomnia, depression, anger, headache, etc.), these two herbs have very good effects.
Nojourni et al., 2016 (35)	Sertraline 50 mg/day Passion Flower (passiflora) Placebo	30	Anxiety	Double-Blind placebo-controlled study	This study noted that passionflower (passiflora) might be suitable as an add-on in the treatment of generalized anxiety disorder with low side effects.
da Silva et al., 2017 (25)	Placebo or experimental single dose or passiflora Vs. Placebo or experimental multiple doses of passiflora	90	Anxiety	Double-blind placebo-controlled trial	It is suggested that supplementation using Passiflora incarnate L. Capsules (500 mg) decreased cardiovascular signals both in single and in multiple doses, associated with the stress of public speaking.
Hubner et al., 2009 (26)	Homeopathic preparation Neurexan vs. combination formulations based on valerian extracts	826	Nervousness and restlessness	Prospective, nonrandomized, no interventional, observational study	Neurexan appears to be an effective and well-tolerated alternative to valerian-based combination therapies for the treatment of nervousness/restlessness
Takara et al., 2019 (27)	Passion flower (passiflora) extract	44	Anxiety	Randomized, placebo-controlled, double-blind trial	Passionflower (passiflora) extract is effective in improving anxiety.
Halder, 2016 (28)	Homeopathic Individualized C-Potencies Vs. Fluoxetine or Placebo	189	Moderate to severe depression	Randomized, placebo-controlled, double-blind	Results were inconclusive due to certain reasons
Movafegh et al., 2008 (29)	Passiflora incarnate And Placebo	60	Anxiety of surgery	Double-blind Placebo-controlled study	Outpatient surgery, administration of oral Passiflora incarnate as a premedication reduces anxiety without inducing sedation.
Ghamchini et al., 2019 (30)	Chamomile tea	110	Anxiety and Depression	Single blind clinical trial	Chamomile tea can be used as an alternative treatment to depression therapy in cancer patients Undergoing chemotherapy due to its low, safe, simple and affordable side effects

Biswas et al., (31)	Homeopathic medicines	30	Depression with suicidal tendency	Prospective study	Homeopathic medicines are efficacious in depression when chosen carefully
Villet et al., 2016 (32)	Passiflora composita	639	Anxiety and sleep disorder	Open-label observational study	Anxiety and/or SDS improved significantly in patients included in this study. Passiflora composita could be an alternative to the use of psychotropic drugs for first intention treatment of anxiety and SDS
Katz, et al., 2005 (33)	Fluoxetine Vs individualized homeopathic medicines	31	Depression	Randomized placebo-controlled clinical trials	A trial of this design in general practice is not feasible, because of recruitment difficulties, many of them linked to patient preference. Different approaches are required to recruit adequate patient numbers to trials of this sort.
Bonne et al., 2003 (34)	Individualized homeopathic remedy Vs. Placebo	44	Anxiety disorder	Double-blind placebo-controlled study	The effect of homeopathic treatment on mental symptoms of patients with generalized anxiety disorder did not differ from that of placebo. The improvement in both conditions was substantial.

Table 2: Clinical Trials Related To Depression

treatment of anxiety and depression. For this purpose, full-length papers were studied related to anxiety, depression, and sleep disorders. Articles related to the effectiveness of homeopathic medicines for depression and anxiety were searched because depression is the condition for which most of the times homeopaths are consulted for (3). Thus, this review aimed to evaluate the efficacy of homeopathic remedies for depression. For this purpose, an extensive literature search was carried and total 60 articles were found. Irrelevant articles were excluded. Only 22 articles were included which were according to the inclusion criteria.

A cohort multiple randomized controlled trial was designed to evaluate the efficacy of homeopathic medicines provided by homeopaths for self-reported depression. Homeopathic medicines were found to be effective and acceptable in patients with depression but more refined studies should be conducted to strengthen these results (3). A prospective, randomized, double blind double dummy trial was conducted to evaluate the efficacy of individualized Q potencies in comparison to

Fluoxetine. This study revealed that individualized Q potencies were not inferior as compared to Fluoxetine. More studies are needed to authenticate these findings (18). A randomized double blind trial was conducted in Brazilian sample to assess the efficacy of Hypericum in comparison to Fluoxetine for the treatment of mild to moderate depression. Major findings of this trial were that Fluoxetine had better results than Hypericum in mild to moderate depression but both medicines were safe and well tolerated. There is need of more trials on a large sample to confirm these results (20)

On 70 patients, efficacy of Hypericum preparation was evaluated in comparison to Fluoxetine. Hypericum was well tolerated and no adverse effect was noted as in other studies. Some adverse effects i.e. headache, nausea, diarrhea, dry mouth, anxiety/nervousness were reported in other studies (21). A randomized, placebo-controlled, double blind, double dummy, superiority, three-arm trial was conducted in patients with moderate to severe depression. Major findings of this study were that individualized Homeopathic

treatment (IHT) and Fluoxetine were effective in the treatment of depression in climacteric women. Well designed randomized clinical trials are needed to evaluate the efficacy of homeopathic remedy deeply (22). A randomized controlled trial was conducted in patients with depression to evaluate the efficacy of Hypericum. In this study, Hypericum failed to prove its efficacy in patients with moderate to severe depression. (17).

EPI3 cohort studies revealed that patients with anxiety and depression disorder chose to consult physicians who administered homeopathic medicines with conventional medicines. Patients with anxiety and depressive disorders reported less use of psychotropic drugs and showed good clinical improvement than patients used conventional medicines. One of the major limitations of this study was a low participation rate. (19). A prospective, non-comparative, open-label observational study was carried out to evaluate the role of homeopathic medicines in depressive disorders. This study concluded that homeopathic medicines showed significant results in depression symptoms. As compared to controlled trials, it was a weaker study.

That is why further studies should be controlled to assess the efficacy (16).

Adler designed a double blind placebo controlled trial in patients with mild to moderate depression. Results of this study were inconclusive because due to some limitation study was terminated before completion. Small sample size, a long list of exclusion criteria were the major drawbacks of this study. Patients were enrolled in this study only after psychiatric diagnoses which complicated the whole process of recruitment (15). Another randomized double-blind placebo controlled study was conducted to evaluate the effects of homeopathic medicines in reducing the symptoms of anxiety and depression disorder. This study revealed that homeopathic medicines can be used to treat anxiety and depression disorders. (23).

A comparative study conducted by Fahami on 59 women of menopausal age. According to this study, both

Hypericum perforatum and passionflower (passiflora) found to be effective in reducing the menopausal symptoms. Placebo controlled trials must be conducted to draw more accurate results (24). Another study was conducted in patients with generalized anxiety disorders. Total 30 patients were enrolled in this study and the good effects of passion flower (passiflora) were seen. Small sample size, short duration of the study, and lack of structured interviews were the major limitations of this study. (35).

To reduce generalized anxiety disorders, *passiflora incarnata* had used and very good results were seen in the patient. It was seen that supplementation using *passiflora* decreased cardiovascular signs in both single and in multiple doses (25). While another study concluded, *passiflora* was useful for decreasing anxiety and no adverse effects were found. In traditional medicines, *passiflora* has been used for sedatives and anxiolytic purpose (27). A double blind placebo controlled study was conducted in patients with pre-operative surgery. No adverse effects were noted during this study. Total 60 patients were enrolled in this study, which was a very small sample size. In this study, it was seen that the administration of oral *passiflora* helped to reduce pre-operative anxiety (29).

A trial on 639 patients in 22 regions of France was conducted and this study showed the effectiveness of *passiflora* in decreasing the anxiety and sleep disorder. It was an open label observational study. It was also noted that *passiflora* was well tolerated than other psychotropic drugs. Further trials are needed to authenticate these findings (32). A comparative study on 826 patients with Neurexan homeopathic preparation and the valerian-based combination was conducted which resulted in the effectiveness of homeopathic preparation Neurexan in treatment of anxiety and nervousness. It had also very good effects on their general health. Neurexan has also substances of *passiflora* in it. Limitation of the study was the absence of placebo group as it was non interventional study and



another disadvantage was lack of blinding and randomization (26).

Halder had conducted the study on 189 peri and post menopausal women. The findings of this study were non-conclusive because some time homeopathic medicines take more time to show results so the design of this trial was not suitable in this regard (28). Chamomilla tea was given to cancer patients who suffered from depression and very positive results were seen. It had reduced depression in cancer patients. It was recommended because it is safe and effective (30). Depression affects millions of people globally; it is a state of mind, body, and thought, which work together towards negativity (36)

A Prospective single blind placebo controlled study concluded that homeopathic medicines had a very good effect on depression; in patients suffered from depression with a suicidal tendency (31). A Randomised, double dummy, double-blind parallel group clinical trial was conducted in 31 patients to treat depression. Individualized homeopathic medicines and Fluoxetine were given to patients but no solid conclusion was obtained. Major drawbacks of this trial was the design of this study, patients preferences regarding medicines, improper recruitment method and insufficient sample size (33). Bonne conducted a double blind placebo control study on 44 patients to assess the effectiveness of homeopathic medicines over placebo in the treatment of depression. Improvement was noted in both homeopathic and placebo group. Duration of the trial was very short as homeopathic treatment sometimes require longer period of time (34).

## CONCLUSION

This systematic review concluded that homeopathic medicines are effective in the treatment of anxiety, depression and psychic problem. However, it is need of the hour to conduct more randomized placebo control trials to strengthen the evidence. In future studies should be conducted for long duration, as sometimes-homeopathic medicines require long time to

cure the symptoms completely.

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