

## EFFICACY AND SAFETY OF ANTISCABIETIC AGENTS : A SYSTEMATIC REVIEW

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### ABSTRACT

*Scabies is a contagious skin condition that is caused by a mite called *Sarcoptes scabiei*. This mite burrows into the skin and causes a severe itching sensation. Scabies can be spread either directly from person to person through scratching or indirectly through contact with contaminated surfaces or objects (fomites). Due to the fact that many people may only exhibit mild symptoms, accurate diagnosis of this ailment can be challenging at times. Scabies can be effectively treated with a variety of different medications. However, clinical trials comparing the efficacy of these treatments, in particular the available topical agents, are relatively few in number. As a consequence, prescribing practice varies greatly from country to country and is largely determined by factors such as the cost and availability of treatments as well as the individual preference of the treating physician. Permethrin, oral ivermectin, and synergized pyrethrins appeared to provide the best balance between these two outcomes compared to the other treatments. These three treatments were located closer to the right upper corner of the clustered ranking plot than the other treatments. On the other hand, the fact that the adverse events (AEs) that were reported in these trials were not serious adverse reactions (such as hospitalization or death) means that one could rationally give them less weight than the cure. Our study found that ivermectin and permethrin were the most effective treatments. The antiscabietic agents used in this study had few or manageable adverse effects, and the study did not find any severe adverse effects.*

**Keyword:** *Antiscabietic agent; Ivecmetrin; Primetherin; Scabies*

## INTRODUCTION

Scabies is an infectious skin disorder caused by the mite *Sarcoptes scabiei*, which burrows into the skin and produces intense itching. Scabies is transferred through direct skin-to-skin contact or through indirect contact with contaminated objects (fomites). Often, it is difficult to diagnose this ailment because many people may exhibit only modest symptoms. Other patients, however, may present with the characteristic exposure history, severe pruritis that is exacerbated at night, and references to other individuals with similar symptoms.<sup>1,2</sup> *Sarcoptes scabiei var. Hominis* is the mite that causes scabies. This arthropod belongs to the *Acarina* order. It belongs to the *Arachnida* class, the *Astigmata* order, and the *Sarcoptidae* family.<sup>3</sup>

The mite *Sarcoptes scabiei* inhabits the dermal and epidermal layers of both humans and animals. Scabies is a frequent and universal skin disorder. The female mite begins the infestation by burrowing into the stratum corneum of its victim, where she deposits her eggs. It subsequently transforms into larvae, nymphs, and adults. A person with the classic form of scabies may have a mite population ranging from 10 to 15 organisms.<sup>2</sup> In cases of classic scabies, it normally takes 10 minutes of skin-to-skin contact for mites to spread to another human host. The disease can also be transmitted via fomite transmission on clothing or bed sheets.<sup>4,5</sup> This presentation of scabies typically presents as diffuse or localized hyperkeratotic plaques on the palms, soles, and under fingernails. The nodular form of scabies differs from the traditional version.<sup>6-8</sup>

Scabies can be treated in a variety of ways. When medications are taken as prescribed, the efficacy of standard treatment options is comparable. Topical permethrin, topical crotamiton, and systemic ivermectin are examples of these. Adverse reactions to these medications are uncommon.<sup>7</sup> Many medications have been used to treat scabies, but it is unknown which one is the most effective. In this review of the relevant literature, we will present study that demonstrates the efficacy and safety of antiscabietic agent.

## METHODS

The full-text papers written in English were used as the source material for the data that was gathered for the purpose of conducting this systematic review. The main objective of this systematic review was to demonstrate efficacy of antiscabietic agent, and safety antiscabietic agent for secondary objective. Pubmed and Google Scholar are the two databases that were employed during the production of this essay. In this inquiry, the PICO analysis was used to scabies patient. Efficacy and safety antiscabietic agent as the index and without comparisons. As component elements, the research included both controlled clinical trials and randomised clinical trials as part of it.

The keywords used in the search were “antiscabietic agent” “safety” and “efficacy”. We include study conducted above in 2012-2022. This analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) paradigm, in which the researchers originally entered keywords into each database. The phrases : ("antiscabietic"[All Fields] AND ("agent"[All Fields] OR "agents"[All Fields]) AND ("efficacies"[All Fields] OR "efficacious"[All Fields] OR "efficaciously"[All Fields] OR "efficaciousness"[All Fields] OR "efficacy"[All Fields]) AND ("safety"[MeSH Terms] OR "safety"[All Fields] OR "safeties"[All Fields])) AND (y\_5[Filter]) used in this study. We received four articles, which will be discussed during the discussion (Table 1).

## RESULT

Rezaee *et al* (2015) conducted a study with sixty patients and family members were given 5% permethrin cream, while the other 60 were given 1% lindane lotion. The treatment was evaluated at 2 and 4 week intervals. After two weeks, permethrin improved 48 patients (80%), whereas lindane improved only 28 patients (46.6%).<sup>9</sup> Second study from Ahmad *et al* (2016) showed majority of patients (87.5% in group topical ivermectin and 73.5% in oral ivermectin) were symptom free. Four patients in Group I and eight patients in Group II required a second treatment. However, two weeks after treatment, all symptoms and signs had completely resolved, with no recurrence at four weeks. Topical and oral ivermectin are safe and effective for treatment of scabies. A single treatment, whether topical or oral is associated with a high cure rate in one week. However, resuming treatment after one week may be necessary to achieve complete cure.<sup>10</sup> Alipour *et al* (2015) showed a single dose of ivermectin provided a cure rate of 61.9% at the 2-week follow-up, which increased to 78.5% at the 4-week follow-up. At the 2-week follow-up, treatment with single applications of sulfur 10% ointment was effective in 45.2% of patients, increasing to 59.5% at the 4-week follow-up after this treatment was repeated. At the 2-week follow-up, a single dose of ivermectin was as effective as single applications of sulfur 10% ointment. At the 4-week follow-up, ivermectin was superior to sulfur 10% ointment after the treatment was repeated.<sup>11</sup>

**Table 1. The literature include in this study**

Author	Origin	Method	Sample Size	Period	Agent	Result
Rezaee, 2015 <sup>9</sup>	Iran	RCT	120 patients	2-4 weeks	Lindane 1% vs permethrine 5%	Permethrin (5%) cream was found to be significantly more effective than lindane in the treatment of scabies. Adverse reactions were uncommon in both the permethrin and lindane groups.
Ahmad, 2016 <sup>10</sup>	Egypt	RCT	62 patients	1-4 weeks	Oral vs topical ivermectin	Topical and oral ivermectin are safe and effective in the treatment of uncomplicated scabies. A single treatment, whether topical or oral, is associated with a high cure rate in one week. However, resuming treatment after one week may be necessary to achieve complete cure.
Alipour, 2015 <sup>11</sup>	Poland	RCT	420 patients	2-4 weeks	Oral Ivermectin and sulfur 10%	At the 4-week follow-up, ivermectin was superior to sulfur 10% ointment after the treatment was repeated.
Goldust, 2014 <sup>12</sup>	Iran	RCT	320 patient	2-4 weeks	Oral ivermectin and Crotamiton 10%	At the two-week follow-up, a single dose of ivermectin was as effective as one application of crotamiton 10% cream. At the four-week follow-up, ivermectin was superior to crotamiton 10% cream after repeat treatment. The delay in clinical response to ivermectin suggests that it may not be effective against all stages of the parasite's life cycle.

Goldust, *et al* (2014)<sup>12</sup> showed a single dose of ivermectin provided a cure rate of 62.5% at two-week follow-up, which increased to 87.5% at the four-week follow-up after the treatment was repeated. At the two-week follow-up, crotamiton 10% cream was effective in 46.8% of patients, increasing to 62.5% at the four-week follow-up after this treatment was repeated. Ivermectin proved to be more effective than crotamiton 10% cream at the four-week follow-up after receiving multiple treatments. The fact that the clinical response to ivermectin was so slow to materialize raises the possibility that the medication is not effective against all phases of the parasite's life cycle.

## DISCUSSION

The mite *Sarcoptes scabiei* is the vector for the parasitic infection known as scabies, which affects the skin. Scabies outbreaks are common in residential and nursing care homes in developed countries, where they are responsible for a significant amount of morbidity and distress.<sup>13</sup> Children, adolescents, and the elderly make up the majority of those who are diagnosed with this condition. Scabies is still a major public health concern in some regions, where it affects more than half of the population and continues to spread rapidly. Estimates from around the world range anywhere from 200 million to 300 million cases at this time.<sup>14</sup>

The first step in the life cycle of the scabies mite, also known as *S. scabiei* var. *hominis*, is for the pregnant female to burrow into the epidermis of a human and lay between two and three eggs per day. After 48–72 hours, the larvae will emerge and begin to form new burrows. In ten to fourteen days, the larvae develop into adulthood, mate, and the life cycle begins again.<sup>15</sup>

Transmission requires direct skin-to-skin contact between infected individuals. Mites that cause human scabies are able to live in the environment, away from the host human body, for up to 24–36 hours at temperatures as high as 21°C and relative humidity ranging from 40–80%.<sup>16</sup> During this time, the mites are still capable of infesting humans. It has been suggested that transmission can occur indirectly, such as through clothing, bedding, and other fomites; however, this has been difficult to demonstrate experimentally.<sup>17,18</sup>

Mellanby's experiments demonstrated that indirect transmission is not likely to play a significant role, with the possible exception of crusted scabies cases in which the host is heavily infected. In their studies, volunteers slept on mattresses and pillows that had been used by people who had scabies within the previous twenty-four hours. Only 1.3% of the volunteers, or 4 out of 300, became infected with the parasite when the patients had parasite rates between 20 and 50.

When the patients had parasite rates of 200 or higher, thirty percent of the volunteers (three out of ten) became infected with the parasites.<sup>2,19</sup>

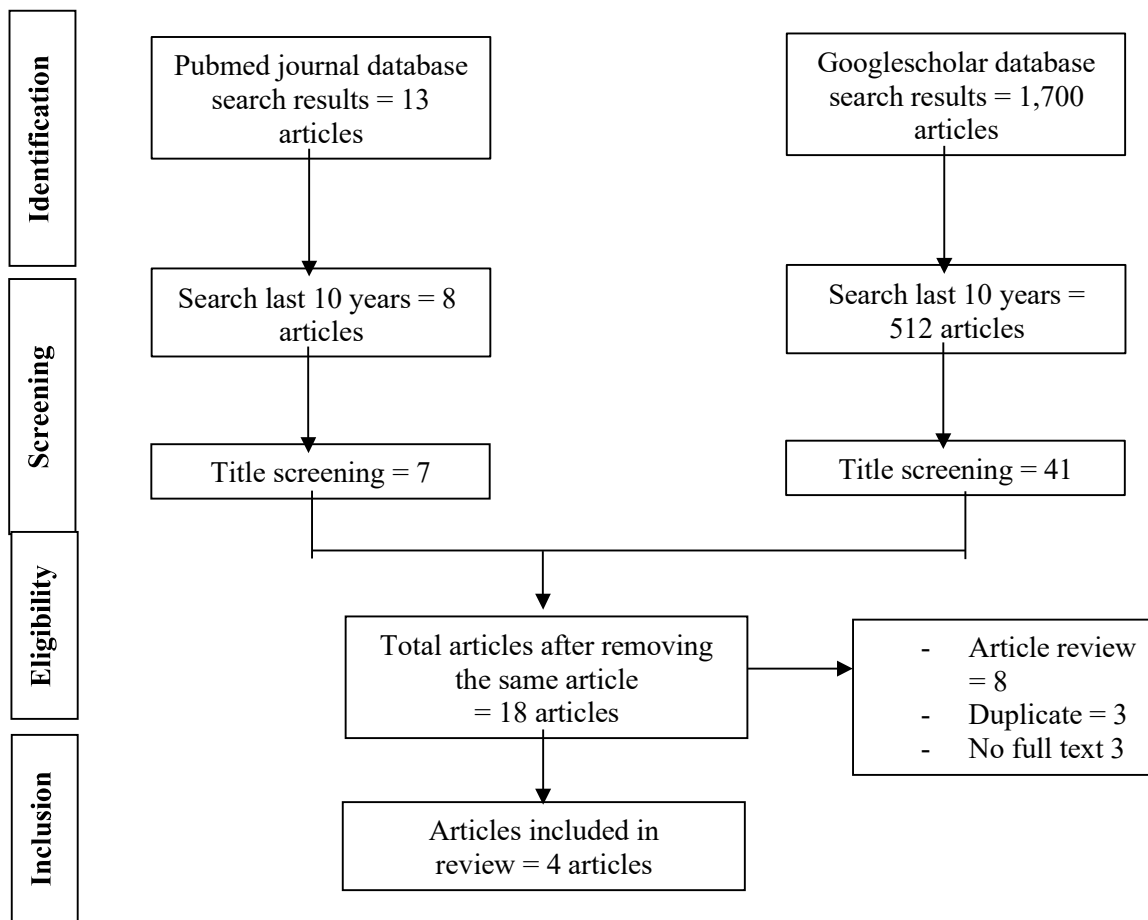


Figure 1. Article search flowchart

Scabies can be effectively treated with a variety of different medications. However, clinical trials comparing the efficacy of these treatments, in particular the available topical agents, are relatively few in number. As a consequence, prescribing practice varies greatly from country to country and is largely determined by factors such as the cost and availability of treatments as well as the individual preference of the treating physician. The level of diagnostic certainty will play a role in determining individual case management. This level of certainty may take into account a wide range of differential diagnoses depending on patient and geographic factors.<sup>2,19</sup>

Although the consensus criteria for the diagnosis of scabies from 2018 may be helpful for guiding case management by non-expert health workers, they will be more relevant as a tool for use in research studies and mass treatment programs, in which the diagnostic hierarchy may be used to identify suitable or comparable populations. It is important that individual cases of "suspected" scabies be treated as though they are true cases of scabies; in other words, treatment should not be limited to only those who have a diagnosis of "clinical" or "confirmed" scabies.<sup>2,19</sup>

Our research found that ivermectin and permethrin were the most effective treatments.<sup>9-12</sup> When compared to permethrin 5% cream, ivermectin taken orally (at a standard dose of 200 µg/kg) may result in slightly lower rates of complete clearance after one week. In the trials with permethrin, the average clearance rate was 65%. The illustrative clearance with ivermectin is 43% (RR 0.65, 95% CI 0.54 to 0.78; 613 participants; low-certainty evidence). However, by week two, there may be little to no difference (illustrative clearance of permethrin 74% compared to ivermectin 68%; relative risk (RR) 0.91, 95% confidence interval (CI) 0.76 to 1.08; 459 participants, 5 studies; low certainty evidence).<sup>20</sup> Oral ivermectin is recommended in situations in which topical treatments have failed, in patients who do not adhere to topical treatments, in patients who are unable to apply topical treatments (people who are physically or mentally disabled, refugees, or the homeless), in widespread institutional outbreaks, in mass populations, and in patients whose scabies have crusted over. Ivermectin is extremely safe, and dosing can be off by up to three times the recommended amount without causing any problems. Side effects at these doses are uncommon and difficult to differentiate from the

symptoms of the disease and anxiety, but they can include headaches, nausea, dizziness, and upset stomachs. It is believed that the death of mites, rather than the drug itself, is the cause of many of the adverse effects.<sup>7,20,21</sup>

Treatments with one to three doses of ivermectin or one to three applications of permethrin may lead to little or no difference in rates of complete clearance after four weeks of follow-up (illustrative cures with one to three applications of permethrin 93% and with one to three doses of ivermectin 86%; relative risk (RR) 0.92, 95% confidence interval (CI) 0.82 to 1.03; 581 participants, 5 studies; low certainty evidence. After one week of treatment with oral ivermectin at a standard dose of 200 µg/kg or one application of permethrin 5% lotion, there is probably little or no difference in complete clearance rates (illustrative cure rates: permethrin 73%, ivermectin 68%; RR 0.93, 95% CI 0.74 to 1.17; 120 participants, 1 study; moderate-certainty evidence). After two weeks of treatment, one dose of systemic ivermectin compared to one application of permethrin lotion may lead to similar complete clearance rates (extrapolated cure rates: 67% in both groups; RR 1.00, 95% CI 0.78 to 1.29; 120 participants, 1 study; low-certainty evidence).<sup>20</sup>

**Table 2. Efficacy antiscabietic agent**

Study	Agent	Efficacy (%)
Rezaee, 2015	Lindane 1%	46,6
Rezaee, 2015	Permethrine 5%	80,0
Ahmad, 2016; Alipour, 2016; Goldust, 2014	Ivermectin oral	80,0
Ahmad, 2016	Ivermectin topical	87,5
Alipour, 2015	Sulfur 10%	59,5
Goldust, 2014	Crotamiton 10%	62,5

Permethrin, oral ivermectin, and synergized pyrethrins appeared to provide the best balance between these two outcomes compared to the other treatments. These three treatments were located closer to the right upper corner of the clustered ranking plot than the other treatments. On the other hand, the fact that the adverse events (AEs) that were reported in these trials were not serious adverse reactions (such as hospitalization or death) means that one could rationally give them less weight than the cure. Therefore, the combination of permethrin and oral or topical ivermectin, which ranked first and third, respectively, in terms of curing the infection, should still be acceptable.<sup>19</sup>

Some antiscabies medications are linked to significant safety concerns, especially for children.<sup>22</sup> Patients suffering from loiasis and onchocerciasis have been reported to have a significantly increased risk of experiencing serious adverse events (AEs), including encephalopathy and death, after taking oral ivermectin. Despite this, ivermectin is generally regarded as a safe medication to take. There is a possibility that a high microfilarial load, co-infection with other bloodborne parasites, or genetic predisposition are all linked to these serious adverse events (AEs).<sup>23,24</sup>

When compared to sulfur, the use of permethrin carries a significantly lower risk of adverse effects (AEs), whereas synergized pyrethrins carry a higher risk of AEs. Synthetized pyrethrins were found to have an AE risk that was significantly lower than that of sulfur, which was found to have an AE risk that was significantly higher than that of most other agents. It was discovered that synergized pyrethrins had the lowest probability of adverse effects, followed by malathion and then oral ivermectin.<sup>9,11,25</sup>

Clustered ranking was used to evaluate cure at 3-6 weeks as well as adverse events. The combination of permethrin, oral and topical ivermectin, and topical ivermectin received a high ranking for curing the condition, but a much lower ranking for adverse effects. Synergized pyrethrins had the best score for AEs, but they received a slightly lower score for cure. Permethrin and oral ivermectin were ranked highly for their ability to cure the condition while only having moderate adverse effects. Malathion ranked second for AEs, but it had the worst cure rate. The remaining treatments did not stand out, either positively or negatively, in either outcome.<sup>9,11</sup>

Other study reporting of adverse events in studies that were included was less than ideal. There were no withdrawals because of adverse events in either the group receiving systemic ivermectin or the group receiving permethrin (evidence of moderate to high certainty). Two weeks after treatment was first administered, there was probably very little difference, if any difference at all, in the proportion of participants treated with systemic ivermectin or permethrin cream who experienced at least one adverse event.<sup>20</sup>

**CONCLUSION**

Our research found that ivermectin and permethrin were the most effective treatments. The antiscabietic agents used in this study had few or manageable adverse effects, and the study did not find any severe adverse effects.

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