Review Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2023.51.008089

Ozonated Oil for the Treatment of Skin Disorders: A Truth or Myth? : A Systematic Review

Sara Araby[1]*, Mohamed Abdelgaied[1] and Mohamed Solayman[1,2]*

[1]*Clinical Pharmacy Department, Faculty of Pharmacy and Biotechnology, German University in Cairo (GUC), Egypt*

[2]*Clinical Pharmacy Department, Faculty of Pharmacy, Ain Shams University, Egypt*

***Corresponding author:** Sara Araby Ramadan Aly Mosa, Clinical Pharmacy Department, Faculty of Pharmacy and Biotechnology, German University in Cairo (GUC), Egypt

Mohamed Hassan Solayman, Clinical Pharmacy Department, Faculty of Pharmacy, Ain Shams University, Egypt

ARTICLE INFO

Received: June 26, 2023

Published: July 03, 2023

Citation: Sara Araby, Mohamed Abdelgaied and Mohamed Solayman. Ozonated Oil for the Treatment of Skin Disorders: A Truth or Myth? : A Systematic Review. Biomed J Sci & Tech Res 51(2)-2023. BJSTR. MS.ID.008089.

ABSTRACT

Background: Ozonated oils have been proven to have several medical benefits, including stimulation of antioxidant responses, and accelerating wound healing. This systematic review aims to gather evidence on the effect of ozonated oils on different skin disorders.

Methods: Scopus, Sciencedirect, Clinicaltrials.gov, PubMed, Google scholar (the first 10 pages), Researchgate, and Psycinfo were searched. Only randomized control trials (RCTs) in English language using topical ozonated oils as the primary intervention on skin disorders were included in the systematic review. Quality assessment was performed using the National Institute of Health quality assessment tool. Data extraction was done using The Cochrane Collaboration for randomized control trials data collection form.

Results: Out of 1450 search results, eight RCTs that studied the effect of ozonated oils on tinea pedis, vulvovaginal candidiasis, leg ulcers, bedsore, atopic dermatitis, leishmaniasis, and onychomycosis were eligible. Head-to-head comparison of the ozonated oil to the standard of care showed comparable results with higher safety profile. However, two of the studies (one on the onychomycosis and the other on tinea pedis) had the recurrence rate as an additional endpoint and showed positive results to the ozonated oil group compared to the control group.

Conclusion: Ozonated oil shows promising results as a good candidate for the treatment of skin disorders with lower adverse events than the standard of care. However, more studies of larger sample size and longer follow-up periods are needed in order to start using ozonated oil in the clinical practice.

Keywords: Ozonated Oil; Skin Disorders; Atopic Dermatitis; Ulcers; Bedsores; Onychomycosis; Vulvovaginal Candidiasis; Tinea Pedis; Cutaneous Leishmaniasis

Abbreviations: AAD: The American Academy of Dermatology Association; DFU: Diabetic Foot Ulcer; NIH: National Institute of Health; RCTs: Randomized Control Trials; SCORAD: Severity Scoring of Atopic Dermatitis

Introduction

Skin is the largest body organ that plays an influential effect in our lives. It has many essential functions but one of the most important functions is acting like a shield that protects the body's tissues from different threats in the external environment like pathogens, chemical threats, and ultraviolet radiation. As being the barrier to the external environment, skin is exposed to different insults; therefore, skin disorders are very common and considered as high burden [1]. They are the fourth most popular disease that affects the human body, they affect approximately one-third of the population globally [2]. The American Academy of Dermatology Association (AAD) reported that in 2013 nearly 85 million Americans, which is 27% of population visited a dermatologist suffering from skin diseases and the total esti-

mated direct cost of skin disease was nearly $75 billion. Consequently, skin disorders are considered a real threat that requires medical concern. There are several types of skin disorders including diseases of hair, nails, lips, eyelids, external genitalia, and external ear. Examples of skin disorders include acne, atopic dermatitis, cutaneous infections, hair and nail disorders, pruritus, wounds and burns, and many others [3]. For example, acne is a common disorder in which the pores of the skin become blocked which in return cause pimples, black and white heads, and other painful bumps on the skin. Around 80% of people ages 11 to 30 have at least a mild case of acne. Acne affects the quality of life of patients in different forms as it may affect self-esteem and can cause permanent skin damage [4].

Another type is atopic dermatitis, which is the most common chronic inflammatory skin disorder that affects different ages; children and adults [5,6], it causes severe skin dryness, pruritus and skin barrier damage affecting the lives of up to 20% of children and 10% of the adults globally causing sleep disturbances, anxiety, and social withdrawal [7]. Moreover, cutaneous infections which affects around 5.75% of the US population [3] include infections by different kind of germs; bacterial infections like cellulitis, viral infections like shingles and herpes simplex, fungal infections like tinea pedis which is the most common feet disorder and onychomycosis which is a nail disorder [8], yeast infections like vulvovaginal candidiasis, and parasitic infections like body and head lice and scabies [9]. Another type of skin disorder is pruritus which has itchy skin, it has an irritating sensation, it may present as dry itchy skin only while sometimes the skin also is inflamed or has spots or blister and sometimes it gets cracked as well [10]. The last example for skin diseases is wounds that include non-chronic wounds like cuts and scrapes and chronic wound like diabetic foot ulcers, arterial ulcers, pressure ulcers, vasculitic ulcer, non-healing surgical wounds, venous stasis ulcers and others. Ulcers are mainly caused by poor blood circulation [11].

Treatment of skin disorders differs according to the type of skin disease, some diseases respond well to treatment, while the others are chronic diseases in which the treatment only reduce the symptoms if possible [12]. The AAD reported that in 2013 the prescription drugs used in skin diseases cost nearly $15 billion and the cost for OTC products for skin disorders was nearly $10 billion [3]. Ozone (O3) is a gas that was discovered in the nineteenth century. It is composed of three oxygen atoms that are present in a dynamically unstable structure. It acts as a protective barrier from harmful UV radiation, but it was found to have therapeutic effects as well [13]. Ozone was used in the medical field as disinfectant [14] and to decrease the blood cholesterol levels [15], to stimulate the anti-oxidative responses, and to enhance the treatment regime of dental caries [16]. Its efficacy in chronic inflammatory conditions, diabetic foot ulcers, osteonecrosis, and periodontal disease was also reported. Moreover, it is believed to have a potential antimicrobial effect, to activate the immune system and to induce wound healing [14]. Ozone is present as different forms for its medicinal use; ozone gas -it is not inhaled as it has a well-known toxic effect on the respiratory tract in both low and high concentrations [13]-, ozone aqueous solution, ozonated oil, and ozonated water. The other forms of ozone other than the gaseous form were used to get over the instability of the ozone gas in mixture with air. As a result, it was mixed with water or oil to increase its half-life, the ozonated oil has longer half-life than ozonated water [17]. Ozone has the advantages of being effective in wide biological applications, economical, reported to be safe, not only it has a wide spectrum of antimicrobial effect but also has low resistance profile and may lead to a significant decrease of both medical costs and adversities [14]. As a result of the previously mentioned essential effect of ozone, the main aim of this systematic review is to evaluate the present evidence on the efficacy of the ozonated oils in the treatment of skin disorders.

Materials and Methods

Database and Search Strategies

Different common databases were searched; Scopus, Sciencedirect, Clinicaltrials.gov, Pubmed, Google scholar (the first 10 pages), Researchgate, and Psycinfo. The search strategy included both free keywords search and the usage of the following MeSH terms to capture as many studies as possible: ((“Ozonated oil” OR “Ozonized oil” OR “Topical ozone” OR “Ozone therapy” OR “Ozone”) AND (“Skin disorder” OR “ Skin Inflammation” OR “Ulcers” OR “ acne” OR “Skin infections” OR “Wounds” OR “ dermatitis” OR “Alopecia” OR “Psoriasis” OR “Vitiligo”) AND (“ Prognosis” OR “ Healing” OR “ Cure” OR “ Progression” OR “ Size” OR “ Efficacy” OR “ Adverse events” OR “ Side effects” OR “ Safety”)). Two authors (SA and MA) searched and screened all the citations independently.

Inclusion Criteria

Study Design: Only randomized control trials (RCTs) were included in our research applying language filter in which only English language studies were included.

Participants: Human participants were included of any age and gender that were suffering from any skin disorder including ulcers, dermatitis, wounds, infection, inflammation, psoriasis, acne, alopecia, and vitiligo.

Interventions: Topical ozonated oil as the primary intervention whether was administered alone or in combination with any topical or systemic treatment. Only marketed ozonated oil products or ozonated oil that has standardized preparation method and assessed with a method of quality check were included.

Exclusion Criteria

Study Design: Any other study type other than RCTs was excluded like case reports, case studies, observational studies, retrospective studies, preclinical studies, and review articles were excluded.

Participants: Patients with any dentistry related disease or palatal fields were excluded.

Interventions: Studies included gaseous ozone or ozonated water as main interventions were excluded

Other Reasons: abstracts and conference articles with not enough data to extract were excluded.

Study Selection and Data Extraction

Two researchers (SA and MA) read the title, abstract, and full text of the research papers and selected the eligible literature based on the inclusion and exclusion criteria independently. A data collection form that was developed by The Cochrane Collaboration for randomized control trials was used to extract different fields; the first author name, publication date, country, number of participants, different types of intervention and their application method, the duration of the study, whether a consent form was obtained or not, start and end date of the study, the outcome measures, key conclusions of the study and the funding sources. The data extraction was carried out by each of the two researchers (SA and MA) independently and a discussion with a third researcher (MS) took place in case of discrepancies.

Quality Assessment

Two authors (SA and MA) used the National institute of health (NIH) quality assessment tool to assess the quality of the eligible studies on certain domains: the randomization, the generation of the random sequence (selection bias), blinding of the participants and personnel, the similarity between the two arms at the baseline, the drop-out rate at the end of the study, the avoidance of other interventions in the groups and the validity of the outcome measures used and whether they were pre-specified or not.

Results

The search strategy yielded 1450 articles. This was followed by duplicates removal and then screening for relativity to the search and the eligibility criteria. Afterwards, full texts were screened for eligibility, which resulted in only eight studies (7,18,19,20,21,22,23,24) to be included in the quality assessment (Table 1) and the systematic review (Figure 1).

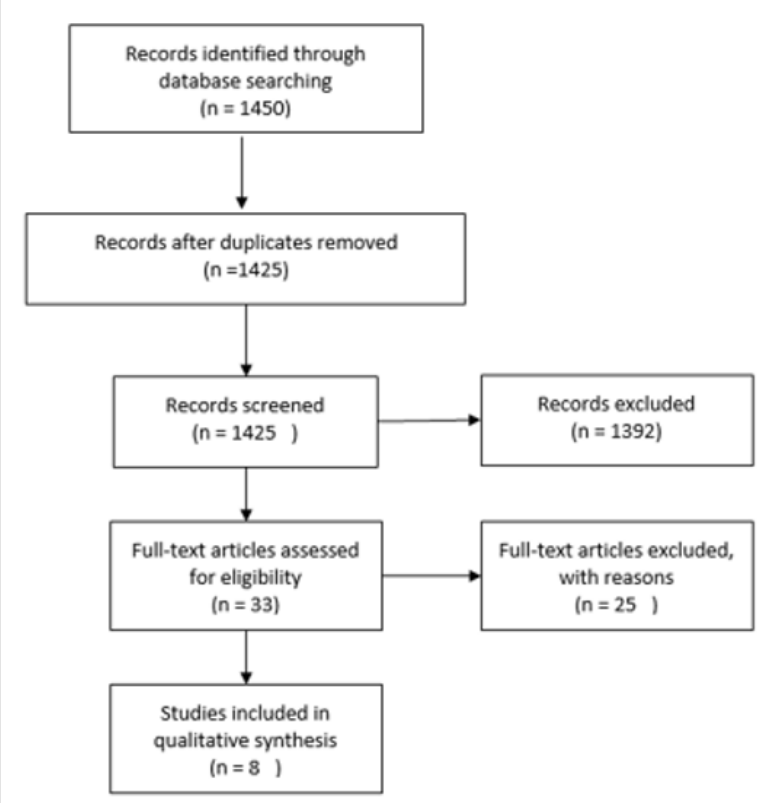

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) flow chart for the steps of the systematic review

Reasons include using oxygen gas not oil, Quasi-experiment, abstract only and insufficient data available, case series and very small sample size (2 patients)

Table 1: Quality assessment result for the eight selected articles.

	Efficacy of a Dermatological Gel Based on Ozonized Sunflower Seed Oil (Oz. Or Oil 30) on Bedsores: A Pilot Study [18]	Efficacy of Combination of Ozonated Water with Oil for Treatment of Tinea Pedis [19]	Efficacy of Comprehensive Ozone Therapy in Diabetic Foot Ulcer Healing [20]	The Effects of Ozonated Olive Oil and Clotrimazole Cream for Treatment of Vulvovaginal Candidiasis [21]	Topical Ozone Therapy Restores Microbiome Diversity in Atopic Dermatitis [7]	The Therapeutic Effect of Ozonated Olive oil Plus Glucantime on human cutaneous leishmaniasis [22]	Efficacy of ozonized sunflower oil in the treatment of tinea pedis [23]	Therapeutic efficacy of topical OLEOZON in patients suffering from onychomycosis [24]
1.Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	N/A	Yes	N/A	N/A	N/A	N/A	N/A	N/A
3. Was the treatment allocation concealed (so that assignments could not be predicted)?	N/A	Yes	No	No	No	No	N/A	N/A
4. Were study participants and providers blinded to treatment group assignment?	No	Yes	No	No	No	No	N/A	Yes
5. Were the people assessing the outcomes blinded to the participants' group assignments?	No	Yes	No	No	No	No	N/A	No
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	No	Yes	No	Yes	N/a	Yes	Yes	Yes
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	N/A
9. Was there high adherence to the intervention protocols for each treatment group?	Yes	Yes	Yes	Yes	Yes	Yes	N/A	N/A
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	Yes	No	N/A	Yes	N/a	Yes	Yes	Yes
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes

12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	No	No	No	Yes	N/a	No	Yes	Yes
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Study Characteristics

Among all the included eight articles with 1005 participants, the publishing dates ranged from 2001 to 2020. These eight studies covered the following different skin disorders: bedsores, tinea pedis, diabetic foot ulcers, cutaneous leishmaniasis, vulvovaginal candidiasis, atopic dermatitis, and onychomycosis. The duration of the studies varied mainly based on the type of skin disease from three days to six months. The application frequency also varied either once or twice a day (Table 2).

Table 2: Summary of the results of the eight articles.

1st author and year	Country	Informed consent obtained	Number of participants	Skin disorder type	Used ozonated oil	Site of the disease	Enrolment date	End date	Measurement tool	Treatment duration	Method of application	Funding
Fatemeh Tara, et al. 2016 [21]	Iran	Yes	81	Vulvovaginal candidiasis	Ozonated olive oil	Female's genital system	N/A	N/A	-Severity of itching, burning and leukorrhea	1 week	Topical every night	N/A
Francesca Serio, et al.. 2017 [18]	Italy	N/A	22	Bedsores	Ozonated sunflower oil	N/A	Sept. 2016	March 2017	Stage of bedsore	3 weeks	Topical 2 applications per day	N/A
Jinrong Zeng, et al. 2020 [7]	China	Yes	12	Atopic dermatitis	Ozonated camellia oil	Elbow & Axillary fossa	June 2016	June 2018	Severity scoring of atopic dermatitis (SCORAD)	3 days	Ozonated water shower 15 mins/day followed by topical ozonated camellia oil 2 times/day and cotton swabs dipped ibn ozonated water in nasal cavities 10x/day	The New Xiangya Talent Projects, theThird Xiangya Hospital of Central South University and the Science and Health Projects of Hunan Natural Science Foundation

LU Jianyun, et al. 2018 [19]	China	Yes	60	Tinea Pedis	Ozonated oil	Foot	N/A	N/A	Mycological examination	4 weeks	The feet were washed with ozonated water for 10 minutes and immersed in it for 20 minutes and then ozonated oil was applied, once a day	N/A
Maryam Aghaei, et al. 2018 [22]	Iran	Yes	30	Cutaneous Leishmaniasis	Ozonated olive oil	Different Areas	2017	2017	Measurement of the lesion size	8 weeks	Topical ozonated olive oil with glucantime twice daily	N/A
Morteza Izadi, et al. 2019 [20]	Iran	Yes	200	Diabetic foot ulcer	Ozonated olive oil	Foot	April 2016	Nov. 2017	Time needed for wound closure and epithelization	Variable (15-180 days)	Wounds are bagged with ozone gas for 30 minutes and ozonated gel was applied on the wounds every 12 hrs and subcutaneous injection of ozone-oxygen was administered around the wound Mixture of ozone and oxygen were administered rectally or intravenously	No fund received
S. Mene´ndez, et al. 2001 [23]	Cuba	Yes	200	Tinea Pedis	Ozonated sunflower oil	Foot	N/A	N/A	Clinical and mycological cure	6 weeks	Daily topical usage of the oil 2 times per day	The Ozone Research-Center and the Health Ministry of Cuba sponsored the study
Silvia Mene´ndez, et al. 2010 [24]	Cuba	Yes	400	Onychomycosis	Ozonated sunflower oil	Toe-nails and finger nails	N/A	N/A	Clinical and mycological cure	3 months	Daily topical usage of the oil 2 times per day	The Ozone Research-Center and the Health Ministry of Cuba sponsored the study

Discussion

This systematic review studies the efficacy of ozonated oil in treatment of different skin disorders due to its previously mentioned benefits that were proved in preclinical and clinical trials. Extensive search yielded only eight articles that were related to skin disorders and ozonated oil. The articles that were included in this systematic review were randomized control trials and the skin disorders included vulvovaginal candidiasis, bedsores, chronic leg ulcers, diabetic foot ulcers, atopic dermatitis, tinea pedis, leishmaniasis, and onychomycosis. The treatment duration in the included studies was dependent on the type of skin disorders. The overall results were in favor for using the ozonated oil in skin disorders, as no side effects were reported in any of the included studies, it is of lower cost than the other treatments and it is either the same efficacy or better than the standard of care. Some studies had a long follow-up period, and they proved a better effect for the ozone containing treatment. Given the clinical and methodological diversity of the included studies, their results and conclusion could not be combined; therefore, the review is organized as summary of the subgroups statistics.

Vulvovaginal Candidiasis

One study [21] randomized 100 female patients of vulvovaginal candidiasis into two groups, the interventional group was treated with ozonated olive oil, and the other group was treated with clotrimazole cream, both for seven days. The outcomes measured were the severity of itching and the severity of leukorrhea. It was concluded that ozonated olive oil is as effective as clotrimazole cream in the treatment of vulvovaginal candidiasis. However, the ozone group had less burning sensation than the clotrimazole group significantly. Moreover, no side effects were reported for either group. The strength points of this trial are an appropriate sample size, similarity of both groups at baseline, and a low percentage of patients dropping out. However, the limitations of this study were not mentioning the randomization method, being an open-label study, and not having a placebo group.

Bedsores

One study [18] randomized 22 patients with bedsores into two groups, the interventional group was treated with ozonated sunflower seed oil with alpha lipoic acid and vitamin E and the other group was treated with common dermatological gel available commercially indicated for cleansing, scarring of sores and lesions or ulcerative origin. The outcome measured was the stage of bedsore weekly for three weeks. The authors concluded that the ozonized oil reduced the duration needed for the healing of bedsores. In this study, they tried to avoid confounders and other factors that may interfere with the results by avoiding any other oil types in both arms during the study as well as just one investigator is responsible for observation and recording. The limitations of the study are being a pilot study as well as it is open-labeled study.

Atopic Dermatitis

One study [7] randomized 12 patients with atopic dermatitis into two groups, the interventional group was treated with ozonated water shower followed by topical ozonated camellia oil, and the control group was treated with a water shower and basal oil, both for three days. The outcome measured was the disease severity using the scoring system SCORAD and lesional microbiome diversity. The results showed that the topical ozone treatment of atopic dermatitis could rapidly improve the symptoms including relief of itching and reduction of inflammation. The limitations of this study include small sample size, selecting only Staphylococcus aureus as the focus of the study and using a test that underrepresents other bacterial causes of atopic dermatitis like Staphylococcus epidermidis and Propionibacterium.

Leishmaniasis

One study [22] randomized 30 patients with leishmaniasis lesions into two groups, the interventional group received ozone saturated olive oil, and the control group received the same volume of glucantime, both were treated for eight weeks. The outcome measured was the lesion size. The results show that ozone therapy can be used either as monotherapy or in combination with other drugs for repairing lesions of leishmaniasis. This study provides a sufficient follow-up period to ensure the efficacy of ozonated olive oil, but the number of participants is small and not being double blinded study were considered limitations for the study.

Diabetic Foot Ulcers

One study [20] randomized 200 patients suffering from diabetic foot ulcers (DFU) into two groups; the interventional and the control groups. The interventional group received the routine therapy for DFU in addition to local and systemic ozone therapy twice a week until wound closure and epithelization were confirmed by the doctor, the ozone therapy was divided into local therapy through bagging and usage of ozonized olive oil and solution and subcutaneous injection of ozone oxygen around the wound and systemic ozone therapy which was the administration of a mixture of ozone and oxygen through rectal or intravenous administration. While the control group received routine treatment for DFU. The outcome measured was the time needed for the healing of the wound. The results showed that the mean healing time in the ozone-treated group was significantly lower than the mean healing time in the control group and the percentage of patients underwent amputation is higher in the control group than the ozone group. This study is strengthened by using sufficient sample size, blinding the patients to decrease the risk of bias, and testing the efficacy of full ozone therapy (local and systemic). The limitations include using different operators at different centers, not ensuring the same fine conditions for the diabetic patients like standard diabetic shoes for example, which can affect the results of the study.

Tinea Pedis

Two studies were conducted on the effect of ozonated oil against Tinea Pedis, one did not mention which type of oil was used and the other one used ozonated sunflower oil but both used ketoconazole as the control group.

One study [19] randomized 60 tinea pedis patients. They were randomized into two groups, the interventional group was washed with ozonated water for 10 minutes and immersed their feet in ozonated water for 20 minutes then applied ozonated oil, and the other group received naftifine hydrochloride and ketoconazole cream, both for 4 weeks. The outcome measured was the mycological examination result. It was concluded that the use of topical ozone has a positive effect on tinea pedis compared to the use of naftifine hydrochloride and ketoconazole cream and no obvious side effects were reported in the interventional group. This trial has different strengths such as using combination of ozonated water and oil to have the benefit of cleaning out and convergence effect of the water and the benefits of the oil as well. Furthermore, not using any other treatment including the long-term use of corticosteroids during the trial is considered as a point of strength. However, the limitations include not mentioning the type of the used oil and not showing the effect of each ozonated treatment alone.

While the other study, [23] randomized 200 patients. The intervention group included 100 patients and applied oleozon - ozonized sunflower oil - twice daily for 6 weeks. The control group included 100 patients and applied ketoconazole twice daily for 6 weeks. The outcome measured was clinical and mycological cure in both groups. The results concluded that both treatment options ketoconazole and oleozon have the same beneficial effect on tinea pedis patients but after 6 months, a follow-up was done, and it revealed that all oleozon-treated patients were negative in the mycological culture while the control group had 4% recurrence and no side effects was observed in the study. The follow-up results are essential and in favor of oleozon treatment, as 90% of the patients in each group were soldiers who have conditions favorable for fungal growth. This study has many points of strengths as it has a very good follow-up period, the homogeneity between groups, and large sufficient sample size. On the other hand, the limitations of the study include being an open label study and not mentioning the method of randomization.

Onychomycosis

One study [24] randomized 400 onychomycosis patients into two groups. The intervention group included 200 patients who were administered one drop of ozonated sunflower oil in each sick nail twice a day for three months. The control group included 200 patients who were administered topical ketoconazole twice daily for 3 months as well. The outcome measured was the clinical and mycological cure or improvement. The results concluded that the patients treated with ozonated oil were cured in a higher percentage and in less time than those of the control group and there are not any patients who got worse at the end of both treatments. Moreover, the study had a follow-up period of one year, and the percentage of the patients who have had fungal infections was 2.8% of the interventional group and 37.0% of the control group. This study had several points of strengths including many participants, a suitable duration of therapy and a long follow-up period. However, the limitations of the study included being a single blind study and not mentioning the method of randomization.

The included studies had several advantages including exploring different skin disorders, large/ sufficient sample size in most of the trials, using an appropriate control to be compared with, most of the studies ensured that no other treatments other than the used for the study are used, and reliable outcome measures were used. However, some points of weakness were observed in the studies including not using a placebo, which makes the differentiation between the effect of ozone and the effect of the oil itself harder. However, this can be credible as the studies used different types of oils not only one, therefore, the effect is most probably due to the ozone. The other points of weakness included that most of the studies were open label, not mentioning the method of randomization or the sample size calculation as only three out of the eight studies mentioned the method of sample size calculation. It is also important to mention that although there was no time filter in this systematic review, there was not any study found after 2020. However, there were studies on ozonated oils but on other fields not skin disorders. This raises the question whether the studies are enough for skin disorders. And if so, they need to be of higher scale in terms of sample size and follow up period to have more credible results and stronger recommendations to start using it in practice as it has promising effect with many advantages like low cost, easy application, and fewer side effects. The limitation of this systematic review includes using studies that use different basal oils for the ozone. However, trials to use only one type of oil were not possible as this approach yielded a very few numbers of studies that could not lead to a conclusion. Therefore, the solution was to include all the controlled studies that use ozone oil as the main intervention.

Conclusion

The ozonated oil shows a promising effect in the treatment of skin disorders, but it needs more powered trials with a clearer evaluation of the safety of the ozonated oils to start using it clinically in the treatment of skin disorders.

Fund

No funds were received for this review.

Conflict of Interest

The authors declare no conflicts of interest.

Authors contributions

Mohamed Solayman and Sara Araby proposed the idea and designed the whole research. Sara Araby and Mohamed Abdelgaied searched and selected the studies. Mohamed Solayman discussed with Sara Araby and Mohamed Abdelgaied in case of any discrepancy. The data retrieval was done by Sara Araby and Mohamed Abdelgaied. The article was written by Sara Araby and Mohamed Abdelgaied and revised by Mohamed Solayman. All authors approved the final manuscript before submission.

Consent for Publication

Not applicable.

Data Availability

The data that support the findings of this review are available from the corresponding author upon request.

References

1. Pullar JM, Carr AC, Vissers MCM (2017) The Roles of Vitamin C in Skin Health. Nutrients 9(8): 866.
2. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, et al. (2014) The global burden of skin disease in 2010: An analysis of the prevalence and impact of skin conditions. The Journal of investigative dermatology 134(6): 1527-1534.
3. Lim HW, Collins SAB, Resneck JS, Bolognia JL, Hodge JA, et al. (2017) The burden of skin disease in the United States. Journal of the American Academy of Dermatology 76(5).
4. (2023) Acne. Cleveland Clinic.
5. Kim BE, Leung DYM (2018) Significance of Skin Barrier Dysfunction in Atopic Dermatitis. Allergy asthma & immunology research 10(3): 207-215.
6. Nowicka D, Nawrot U (2021) Tinea pedis-An embarrassing problem for health and beauty-A narrative review. Mycoses 64(10): 1140-1150.
7. Zeng J, Dou J, Gao L, Xiang Y, Huang J, et al. (2020) Topical ozone therapy restores microbiome diversity in atopic dermatitis. International immunopharmacology 80: 106191.
8. Aggarwal R, Targhotra M, Kumar B, Sahoo PK, Chauhan MK (2020) Treatment and management strategies of onychomycosis. Journal de mycologie medicale 30(2): 100949.
9. (2019) US National Library of Medicine. Skin infections. MedlinePlus.
10. (2023) Mayo Clinic Staff. Itchy skin (pruritus). Mayo Clinic.
11. (2023) Wound Care. Mayo Clinic Health System, MN, USA.
12. (2023) Skin diseases. Cleveland Clinic.
13. Di Paolo N, Bocci V, Gaggiotti E (2004) Ozone therapy. The International Journal of Artificial Organs 27(3): 168-175.
14. Borges GÁ, Elias ST, da Silva SM, Magalhães PO, Macedo SB, et al. (2017) *In vitro* evaluation of wound healing and antimicrobial potential of ozone therapy. Journal of cranio-maxillo-facial surgery : Official publication of the European Association for Cranio-Maxillo-Facial Surgery 45(3): 364-370.
15. Hernández F, Menéndez S, Wong R (1995) Decrease of blood cholesterol and stimulation of antioxidative response in cardiopathy patients treated with endovenous ozone therapy. Free radical biology & medicine 19(1): 115-119.
16. Holmes J (2003) Clinical reversal of root caries using ozone, double-blind, randomised, controlled 18-month trial. Gerodontology 20(2): 106-114.
17. Radzimierska M, Śmigielski K (2019) Ozone and products of ozonation in medical use. Biomedical Journal of Scientific & Technical Research 17(1).
18. Serio F, Dalba M, Cozzolino G, Idolo A, Grassi T, et al. (2017) Efficacy of a Dermatological Gel Based on Ozonized Sunflower Seed Oil (Oz Or Oil 30) on Bedsores: A Pilot Study.
19. Tara F, Zand Kargar Z, Rajabi O, Berenji F, Akhlaghi F, et al. (2016) The Effects of Ozonated Olive Oil and Clotrimazole Cream for Treatment of Vulvovaginal Candidiasis. Alternative therapies in health and medicine 22(4): 44-49.
20. Izadi M, Kheirjou R, Mohammadpour R, Aliyoldashi MH, Moghadam SJ, et al. (2019) Efficacy of comprehensive ozone therapy in diabetic foot ulcer healing. Diabetes & metabolic syndrome 13(1): 822-825.
21. Aghaei M, Aghaei S, Sokhanvari F, Ansari N, Hosseini SM, et al. (2019) The therapeutic effect of ozonated olive oil plus glucantime on human cutaneous leishmaniasis. Iranian journal of basic medical sciences 22(1): 25-30.
22. Lu J, Guo M, Ligui H, Wu K, Xiang Y, et al. (2018) Efficacy of combination of ozonated water with oil for treatment of tinea pedis. Journal of Central South University. Medical sciences 43(2): 147-151.
23. Menéndez S, Falcón L, Simón DR, Landa N (2002) Efficacy of ozonized sunflower oil in the treatment of tinea pedis. Mycoses 45(8): 329-332.
24. Menéndez S, Falcón L, Maqueira Y (2011) Therapeutic efficacy of topical OLEOZON® in patients suffering from onychomycosis. Mycoses 54(5): e272-e277.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.51.008089

Sara Araby Ramadan Aly Mosa and Mohamed Hassan Solayman.

Biomed J Sci & Tech Res