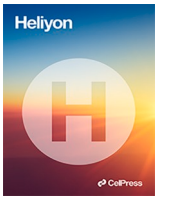
Heliyon 9 (2023) e13253

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Topical Chinese herbal compound in the treatment of oral candidiasis: A systematic review and meta-analysis of randomized controlled trials

Ting Li [a,1], Qiaoyu Hu [a,1], Jiadi Yang [a], Nan Zhang [b], Na Liu [c,**], Qing Liu [a,*]

[a] Hebei Key Laboratory of Stomatology, Hebei Clinical Research Center for Oral Diseases, School and Hospital of Stomatology, Hebei Medical University, Shijiazhuang, 050017, China
[b] Department of Stomatology, Shanxi Bethune Hospital, Third Hospital of Shanxi Medical University, China
[c] Department of Preventive Dentistry, School and Hospital of Stomatology, Hebei Medical University, Shijiazhuang, 050017, China

ARTICLE INFO

Keywords:
Topical Chinese herbal compound
Oral candidiasis
Meta-analysis
Systemic review

ABSTRACT

Objective: A meta-analysis was performed to systematically review the clinical efficacy of external traditional Chinese medicine compounds in the treatment of oral candidiasis to provide a reference for the clinical treatment of this disease.

Methods: We systematically searched relevant Chinese and English databases, including the Chinese Biomedical Literature Database, China National Knowledge Infrastructure, Chinese Scientific Journal Database, Wanfang Database, PubMed, Web of Science, the Cochrane Library and Scopus, from inception to September 2022 to identify all clinical randomized controlled studies of oral candidiasis treated with external Chinese medicine compounds. The inclusion criteria were a randomized controlled study of an experimental group with the intervention of an external traditional Chinese medicine compound, and the results of the literature were clear. Duplicate publications, literature on single or proprietary Chinese medicine treatment, literature from which relevant data could not be extracted and studies without rigorous experimental designs were excluded. Two researchers independently screened relevant studies that met the inclusion and exclusion criteria and conducted quality evaluation and data extraction for the included studies. The total effective rate, Candida negative conversion rate and recurrence rate were statistically analysed by RevMan 5.3 software.

Results: This study included 29 studies and 30 studies, involving 2553 patients with oral candidiasis, with 1320 in the experimental group and 1233 in the control group. The total effective rate of the experimental group was better than that of the control group ($RR = 1.21$ [1.15, 1.27], $P < 0.000$). The negative rate of Candida in the experimental group was better than that in the control group ($RR = 1.25$ [1.05, 1.50], $P=0.01$). The recurrence rate of the experimental group was lower than that of the control group ($RR = 0.34$ [0.18, 0.63], $P=0.0007$). The difference was statistically significant.

* Corresponding author. Hebei Key Laboratory of Stomatology, Hebei Clinical Research Center for Oral Diseases, School and Hospital of Stomatology, Hebei Medical University, No. 383, Zhongshan East Road, Shijiazhuang 050017, PR China.
** Corresponding author. Department of Preventive Dentistry, School and Hospital of Stomatology, Hebei Medical University, No. 383, Zhongshan East Road, Shijiazhuang 050017, PR China.
E-mail addresses: liuna@hebmu.edu.cn (N. Liu), liuqing@hebmu.edu.cn (Q. Liu).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2023.e13253
Received 29 July 2022; Received in revised form 10 January 2023; Accepted 24 January 2023
Available online 26 January 2023

Conclusion: Compared with Western medicine alone, external traditional Chinese medicine in the treatment of oral candidiasis has certain advantages in improving the total effective rate, increasing the negative conversion rate of Candida and reducing the recurrence rate. However, larger samples and high-quality clinical studies are needed to obtain further support and verification.

1. Introduction

Oral candidiasis is a kind of oral mucosal disease caused by Candida infection. It is mainly seen in the "young, old and sick" population. Generally, antifungal agents are used for its treatment. At present, the most conventional and effective drugs for the treatment of oral Candida are polyenes, such as amphotericin B and nystatin; azoles, such as fluconazole, itraconazole, voriconazole and ketoconazole; and echinocandins, such as caspofungin and micafungin [1]. However, traditional antifungal agents, either polyenes, azoles or echinocandins, may produce certain toxic and side effects, recurrence and drug resistance regardless of the form of administration. The incidence rate of the disease and the resistance rate of some strains were increased [2]. Studies have shown that the colonization of oral Candida is closely related to the occurrence of oral cancer [3]. Therefore, it is necessary to find, explore, develop and implement new treatment methods in clinical practice. Traditional Chinese medicine has played an excellent therapeutic role in a variety of diseases, such as skin diseases, stomach diseases, and kidney diseases. However, the treatment of oral candidiasis is controversial, and the evidence concerning the effects has not been fully conclusive. Therefore, this meta-analysis systematically examines the therapeutic effect of relevant topical traditional Chinese medicine compounds on oral candidiasis to provide a reliable evaluation of existing evidence for the clinical treatment of this disease.

2. Materials and methods

2.1. Search strategy

Multiple Chinese and English databases were systematically searched, including the Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP database), Wanfang Database, PubMed, Web of Science, Scopus and the Cochrane Library, from inception to September 2022 to identify randomized controlled trials examining the use of external traditional Chinese medicine for the treatment of oral Candida albicans. The retrieval strategy was mainly composed of MeSH subject words and free words. The search strategies of the relevant English databases were listed in Table 1.

2.2. Inclusion criteria

(1) Types of studies: Randomized controlled study.
(2) Types of Interventions: The experimental group was treated with an external traditional Chinese medicine compound intervention, such as external application and gargle, and dosage forms such as decoction, pill or powder were not limited, and the

Table 1
Complete list of search strategies.

Database/Search engine	Search strategy
PubMed	(((((((((chinese medicine [Title/Abstract]) OR (Medicine, Chinese Traditional [Title/Abstract])) OR (Zhong Yi Xue [Title/Abstract])) OR (single substance drug [Title/Abstract])) OR (traditional Chinese and western medicine [Title/Abstract])) OR (Prescriptions [Title/Abstract])) OR (Prescription [Title/Abstract])) OR (curative effect [Title/Abstract])) AND ((((((((((Candidiasis, Oral [Title/Abstract]) OR (Candidiases, Oral [Title/Abstract])) OR (Oral Candidiases [Title/Abstract])) OR (Oral Candidiasis [Title/Abstract])) OR (oral candidosis [Title/Abstract])) OR (Thrush [Title/Abstract])) OR (Moniliasis, Oral [Title/Abstract])) OR (Moniliases, Oral [Title/Abstract])) OR (Oral Moniliases [Title/Abstract])) OR (Oral Moniliasis [Title/Abstract]))
Web of Science	(TS=(Candidiasis, Oral OR Candidiases, Oral OR Oral Candidiases OR Oral Candidiasis OR oral candidosis OR Thrush OR Moniliasis, Oral OR Moniliases, Oral OR Oral Moniliases OR Oral Moniliasis)) AND TS=(chinese medicine OR Medicine, Chinese Traditional OR Zhong Yi Xue OR single substance drug OR traditional Chinese and western medicine OR Prescriptions OR Prescription OR curative effect)
Cochrane Library	(TS=(Candidiasis, Oral OR Candidiases, Oral OR Oral Candidiases OR Oral Candidiasis OR oral candidosis OR Thrush OR Moniliasis, Oral OR Moniliases, Oral OR Oral Moniliases OR Oral Moniliasis)) AND TS=(chinese medicine OR Medicine, Chinese Traditional OR Zhong Yi Xue OR single substance drug OR traditional Chinese and western medicine OR Prescriptions OR Prescription OR curative effect)
Scopus	(((((((((chinese AND medicine [title/abstract]) OR (medicine, AND chinese AND traditional [title/abstract])) OR (zhong AND yi AND xue [title/abstract])) OR (single AND substance AND drug [title/abstract])) OR (traditional AND chinese AND western AND medicine [title/abstract])) OR (prescriptions [title/abstract])) OR (prescription [title/abstract])) OR (curative AND effect [title/abstract])) AND ((((((((((candidiasis, AND oral [title/abstract]) OR (candidiases, AND oral [title/abstract])) OR (oral AND candidiases [title/abstract])) OR (oral AND candidiasis [title/abstract])) OR (oral AND candidosis [title/abstract])) OR (thrush [title/abstract])) OR (moniliasis, AND oral [title/abstract])) OR (moniliases, AND oral [title/abstract])) OR (oral AND moniliases [title/abstract])) OR (oral AND moniliasis [title/abstract]))

control group was set up. The control measures were clear, including nystatin, fluconazole, ketoconazole, itraconazole and other drug treatments.

(3) Outcome Measures: The literature outcome indicators were clear. The main outcome indicator was the total effective rate, and the secondary outcome indicators were the negative conversion rate and recurrence rate of Candida. The main outcome indicators must be included in each study.

2.3. Exclusion criteria

(1) Duplicate literature.
(2) Literature describing treatments that use a single or proprietary Chinese medicine.
(3) The relevant data cannot be extracted, or the experimental design is not rigorous.

2.4. Literature screening and data extraction

All the retrieved documents were imported into Endnote software for automatic and manual duplication checks. The documents that met the requirements were determined according to the above inclusion and exclusion criteria by reading the title, abstract and full text, which were extracted and analysed by two independent researchers. If they had different opinions on the data and could not make a decision, it was decided by third-party arbitration. The baseline data and outcome indicators in the literature were extracted and drawn into standardized tables. The extracted data included the following: (1) basic information included in the study, e.g., author, year; (2) baseline characteristics and intervention measures of subjects; (3) outcome measures; and (4) composition of traditional Chinese medicine compounds.

2.5. Statistical analyses

Relative risk (RR) was used as the effect value index, and each effect quantity was accompanied by its 95% confidence interval (95% CI). I^2 statistics were used to quantitatively evaluate heterogeneity. If $P > 0.1$ and/or $I^2 < 50\%$, it indicated that the level heterogeneity among the research results was low, and the fixed effects model was used for pooled analysis. If $P < 0.1$ and/or $I^2 > 50\%$, it indicated that there was obvious heterogeneity among the research results, and the random effects model was used for pooled analysis. The potential sources of heterogeneity were examined based on the relevant influencing factors of heterogeneity. The

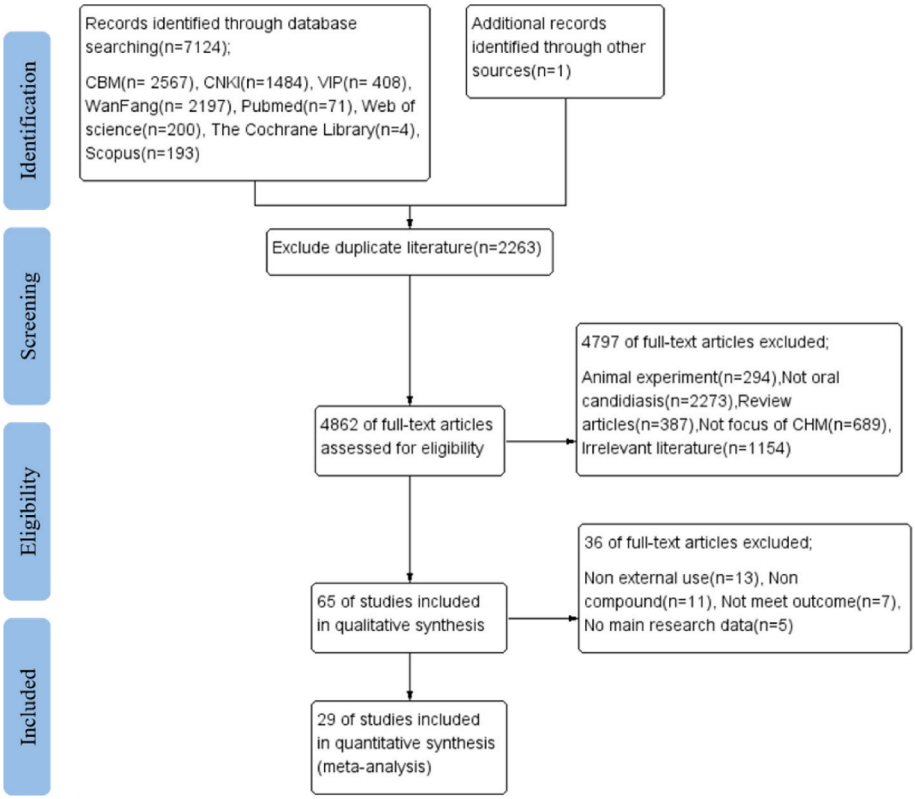


Fig. 1. Flow chart of literature screening.

Table 2
Basic characteristics of the included studies.

NO	Reference	Country	Design	Year	sample size (E/C)	Intervention measures		Treatment time(d)	Outcome Measures
						Experimental	Control		
1	J Cao 2017 [11]	China	Randomized controlled study	2017	47/48	Qingdai Xiaobai San	F + S	14	①②
2	BY Shen 1998 [5]	China	Randomized controlled study	1998	42/36	Qinghuang San + S	N + S	3	①
3	P Chen 2020 [4]	China	Randomized controlled study	2020	40/40	Xiaochuang Powder	N + S	–	①
4	W Chen 2017 [14]	China	Randomized controlled study	2017	30/20	Bingwu San	N	7	①②
5	MF Ding 2017 [13]	China	Randomized controlled study	2017	51/49	Yinqiao Powder	S	–	①②
6	H Fu 2008 [10]	China	Randomized controlled study	2008	50/48	Chinese medicine	N + S	4	①
7	WL Gao 2019 [7]	China	Randomized controlled study	2019	30/30	Bingwu San + N	N	7	①
8	YL Gao 2021 [9]	China	Randomized controlled study	2021	30/30	Chinese medicine + F + S	F + S	14	①
9	XX Lan 2008 [8]	China	Randomized controlled study	2008	35/35	Chinese medicine + S	I + S	7	①
10	GH Li 2021 [12]	China	Randomized controlled study	2021	40/40	Yunv Decoction and Wuwei disinfection drink gargle	S	7	①
11	X Liang 2013 [29]	China	Randomized controlled study	2013	30/30	Chinese medicine	N	5	①
12	R Liu 2019 [6]	China	Randomized controlled study	2019	33/33	Yinlian Decoction	N	5	①
13	WL Nie 2013 [26]	China	Randomized controlled study	2013	132/132	Ejouchuang powder + S	S + N	5	①
14	Y Peng 2017 [25]	China	Randomized controlled study	2017	35/35	Han Dai powder + F + S	F + S	14	①②③
15	C Ren 2015 [22]	China	Randomized controlled study	2015	50/50	Wubai Decoction + F	F	14	①②
16	HY Song 2015 [18]	China	Randomized controlled study	2015	41/41	Rheum officinale + Chinese medicine	N + S	5	①
17	ZJ Song 2020 [17]	China	Randomized controlled study	2020	15/15	Chinese medicine	N + S	–	①
18	CY Wang 2019 [24]	China	Randomized controlled study	2019	50/50	Huanglian and Wubai powder + I	I	7	①③
19	YY Xiong 2018 [28]	China	Randomized controlled study	2018	35/30	Bingwu powder	N	7	①
20	JJ Yang 2015 [16]	China	Randomized controlled study	2015	35/32	Wubai Decoction	F	14	①②
21	J Yang 2015 [16]	China	Randomized controlled study	2015	27/32	Wubai Decoction + F	F	14	①②
22	K Yang 2017 [19]	China	Randomized controlled study	2017	32/32	Chinese medicine + F	F	21	①②
23	LY Yang 2011 [27]	China	Randomized controlled study	2011	50/50	Shenxian Shukou Liquid + I	I	14	①③
24	ZL Zhan 1998 [23]	China	Randomized controlled study	1998	126/65	Qingmei powder	V + VitB + VitC	3	①
25	HW Zhao 2007 [20]	China	Randomized controlled study	2007	32/29	Chinese medicine + S	N	4	①
26	WF Liu 2015 [21]	China	Randomized controlled study	2015	31/31	Chinese medicine + I	I + S	7	①③
27	QT Liu 2001 [15]	China	Randomized controlled study	2001	30/30	Fungal I mixture	S	–	①
28	L Liu 2021 [32]	China	Randomized controlled study	2021	43/43	Jinpu Gargle	S + NS	7	①②
29	GY Kang 2021 [31]	China	Randomized controlled study	2021	48/47	Xiaochuang Powder + N	N	7	①
30	Z Chen 2021 [30]	China	Randomized controlled study	2021	50/50	Chinese medicine	N + S	–	①

Notes: E: Experimental group; C: Control group; F: fluconazole; N: Nystatin; K: Ketoconazole; I: Itraconazole; V: Viocid; S: Sodium bicarbonate; NS: Normal saline. ①: Total effective rate; ②: Candida-negative conversion rate; ③: Recurrence rate.

sensitivity of the research index was analysed by eliminating the literature one by one. When the number of articles was ≥10, a funnel plot was used to detect whether there was potential publication bias.

3. Results

3.1. Literature search results

The initial search yielded 7125 studies. After reading the titles, abstracts and full texts, 7095 studies were excluded, and 29 related studies were ultimately included [4–32] (Fig. 1).

3.2. Basic characteristics of literature

In this study, 2553 patients with oral candidiasis (1320 in the experimental group and 1233 in the control group) were included. Twenty-nine studies were included, and one study compared three experimental groups. Therefore, it was divided into two studies, and thus, a total of 30 randomized controlled studies were included in the current meta-analysis (Table 2).

3.3. Quality evaluation of included trials

All included trials were randomized controlled studies. The quality of the literature included in the study was evaluated according to the evaluation indicators of the Cochrane manual. The word "random" was mentioned in all grouping methods included in the study. Nine studies were grouped using the random number table method [4,7,9,11,13,14,16,27,32]. None of the studies mentioned the method of allocation concealment. Only one study used a blinding method. Most of the study outcome data were complete, and there were no reports of selective outcomes (Fig. 2).

3.4. Outcome measures: total effective rate

The total effective rates of the included studies were compared, and the statistical heterogeneity among the studies was slightly higher (I^2=62%, $P < 0.000$) (Fig. 3). The random effects model was used for pooled analysis. The results of the meta-analysis showed that the total effective rate of the experimental group was better than that of the control group, and the difference between the two groups was statistically significant ($RR = 1.21$ [1.15, 1.27], $P < 0.000$). Subgroup analysis was performed on the main research indices according to drug use. Due to the different medications used in the control group, the patients were divided into the following subgroups: the nystatin group, fluconazole group, itraconazole group, ketoconazole group and nonantifungal drug group. The treatment group was divided into the heat-clearing and detoxifying group, heart and spleen purging group, heat clearing and dampness drying group and deficiency and excess balance group (Table 3). According to the results of each subgroup, although the grouping methods were different and the RR values of each subgroup were also different, the 95% CI range of the combined effect of each subgroup partially overlapped, so it could be considered that there was no difference between each subgroup [33]. The experimental group

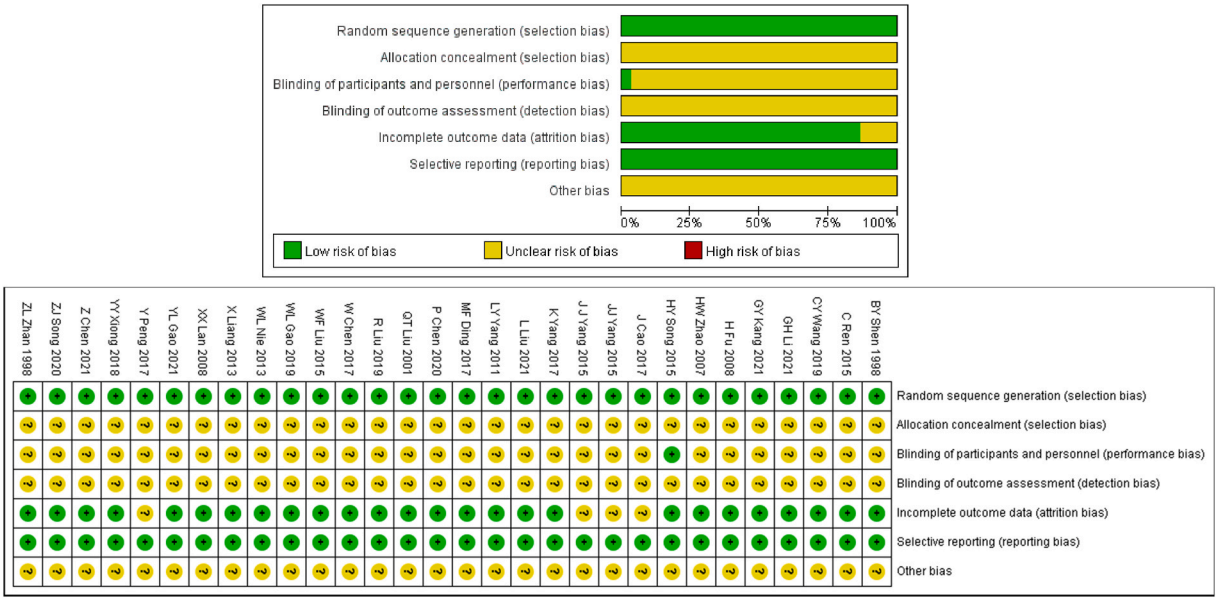


Fig. 2. Treatment evaluation of the literature.

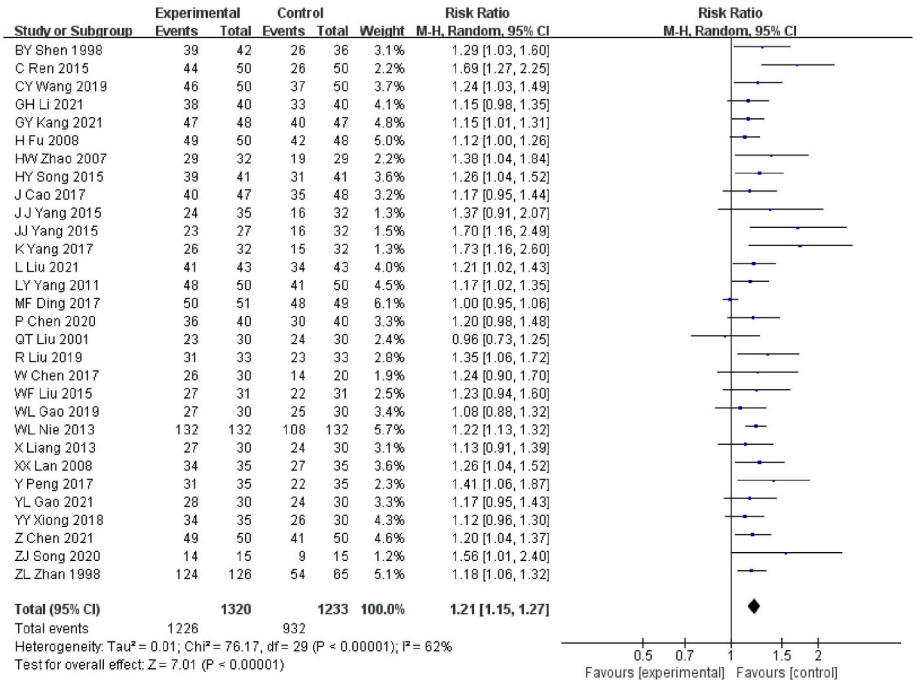


Fig. 3. Comparison of the total effective rate between the experimental and control groups.

Table 3
Subgroup analysis of total effective rate.

Subgroup Name		Number of Studies	Total patients	I^2	*RR*
Subgroup 1	Nystatin group	14	1189	*0%*	*1.19 [1.14, 1.24]*
	Fluconazole group	7	515	*42%*	*1.39 [1.20, 1.60]*
	Itraconazole group	3	262	*0%*	*1.20 [1.08, 1.33]*
	Ketoconazole group	1	70	-	*1.26 [1.04, 1.52]*
	Non-antifungal drug group	5	517	*78%*	*1.10 [0.97, 1.24]*
Subgroup 2	Heat-clearing and detoxifying group	13	1313	*72%*	*1.17 [1.09, 1.27]*
	Heart and spleen purging group	8	598	*0%*	*1.17 [1.10, 1.24]*
	Heat-clearing and dampness drying group	5	376	*23%*	*1.40 [1.20, 1.62]*
	Deficiency and excess balance group	4	266	*31%*	*1.22 [1.06, 1.40]*

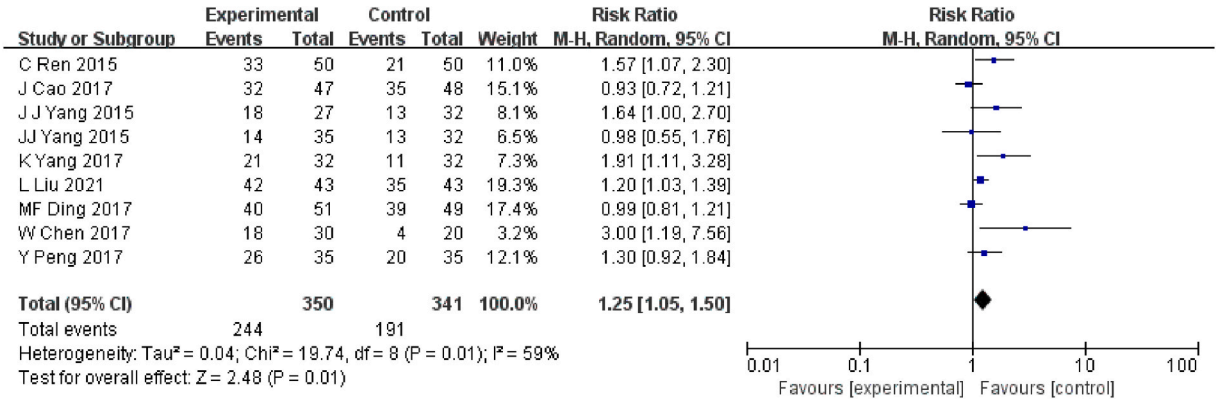


Fig. 4. Comparison of the Candida negative conversion rate between the experimental group and the control group.

treated with traditional Chinese medicine was better than the control group.

3.5. Candida negative conversion rate

Nine studies [11,13,14,16,19,22,25,32] reported the comparison of the Candida negative conversion rate between the experimental group and the control group after treatment. The heterogeneity test results showed that the heterogeneity between studies was acceptable ($I^2 = 59\%$, $P=0.01$), and thus, the random effects model was used for pooled analysis (Fig. 4). Meta-analysis showed that the effect of Candida negative conversion in the experimental group was better than that in the control group, and the difference was statistically significant ($RR = 1.25$ [1.05, 1.50], $P=0.01$).

3.6. Recurrence rate

Four studies [21,24,25,27] reported the comparison of recurrence rate between the experimental group and the control group after treatment. The heterogeneity test results showed that the heterogeneity between studies was low ($I^2 = 0\%$, $P=0.50$) (Fig. 5), and thus, the fixed effects model was used for pooled analysis. Meta-analysis showed that the recurrence rate of patients in the experimental group was lower than that in the control group, and the difference was statistically significant ($RR = 0.34$ [0.18, 0.63], $P=0.0007$).

3.7. Evaluation of publication bias and sensitivity analysis

For the total effective rate of the outcome indicators of more than 10 studies included in this study, the publication bias was analysed by funnel chart (Fig. 6). The funnel plot shows that the scatter points have good aggregation and poor symmetry, so the influence of publication bias cannot be ruled out. The results of the sensitivity analysis showed that after removing the literature one by one, there was no significant difference in the heterogeneity of the statistical results and/or the value of the total effective rate, Candida negative conversion rate or recurrence rate, so the results of this study were relatively stable.

3.8. Chinese herbal medicine frequency

A total of 29 TC M prescriptions were involved in the 29 studies. The TCM prescriptions were exported and named uniformly, and the frequency of medicinal flavours was counted. The 29 prescriptions involved 65 traditional Chinese medicines, with a total frequency of 186 prescriptions. According to the mining method of association rules and the commonly used drug pairs of high-frequency drugs, the drug association network diagram was obtained (Fig. 7).

4. Discussion

Candida is a common oral opportunistic pathogen. When the host defence function decreases, it can invade the human body and cause disease. External use of traditional Chinese medicine can be used locally to reduce gastrointestinal reactions and avoid the first pass elimination effect. This systematic evaluation found that the external use of traditional Chinese medicine in the treatment of oral candidiasis was indeed superior to the simple Western medicine in terms of total effective rate, Candida negative conversion rate and recurrence rate. The differences were statistically significant in each study, and the results were relatively stable, indicating that patients with oral candidiasis are better treated with external traditional Chinese medicine, which can improve the oral state of patients, and the incidence of adverse reactions to traditional Chinese medicine in the study was lower than that to other treatments. Subgroup analysis found that traditional Chinese medicine prescription could achieve similar effective therapeutic effects, whether it is heat clearing and detoxification, purging heart and spleen, heat clearing and dryness and dampness, or both deficiency and excess; compared with nystatin, fluconazole, itraconazole or ketoconazole, traditional Chinese medicine compound has certain advantages in the treatment of oral Candida. According to the current evidence, to a certain extent, the external use of traditional Chinese medicine is effective in the treatment of oral candidiasis, suggesting that in the future, in addition to conventional antifungal treatment, we can also consider the local use of traditional Chinese medicine in the treatment of oral candidiasis.

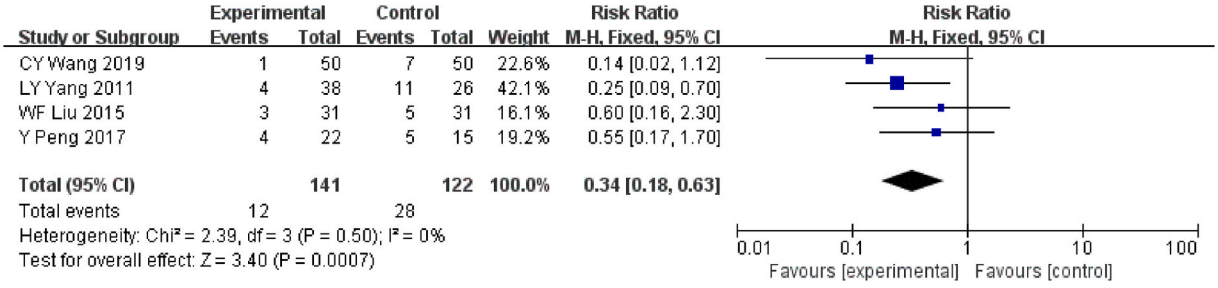


Fig. 5. Comparison of recurrence rates between the experimental group and the control group.

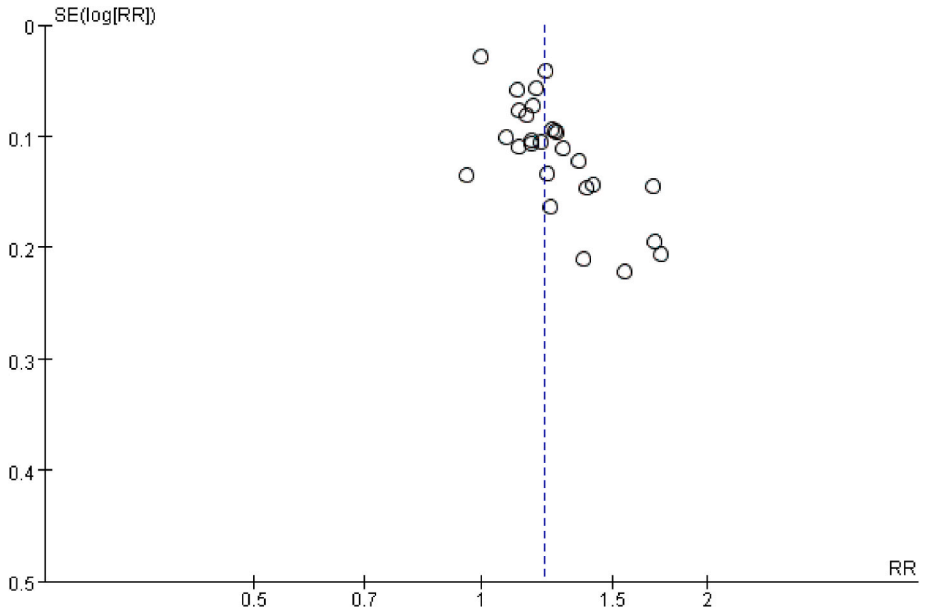


Fig. 6. Funnel diagram of the total effective rate.

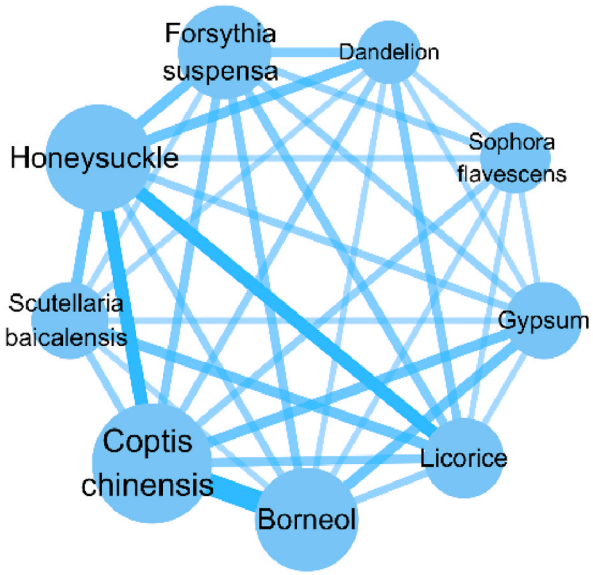


Fig. 7. Frequency distribution of traditional Chinese medicine and Drug Association Network.

The high-frequency and high-correlation drugs in the study were Coptis chinensis, Honeysuckle, Borneol, Forsythia suspensa, Licorice, Gypsum, Scutellaria baicalensis, Sophora flavescens and Dandelion. The first medicine, Coptis chinensis, is a medicine for clearing away heat and detoxification. It is bitter and cold. It can clear away heat, dry dampness, purge fire and detoxify. In an in vitro experiment, Coptis decoction had obvious, stable and effective inhibitory effects on Candida albicans and Candida smooth [34]. Borneol is a resuscitation drug that has a pungent and cool nature and has the effect of clearing heat and relieving pain. At the same time, local administration can promote the absorption of drugs through the mucosa, which can not only absorb rapidly and cause little irritation but also improve the bioavailability of drugs [35]. Honeysuckle, Forsythia and Dandelion suspensa are also heat clearing and detoxifying drugs. Gypsum is a heat clearing powder. Scutellaria baicalensis and Sophora flavescens are medicines for clearing heat and drying dampness. Licorice can replenish qi, strengthen health, and reconcile medicinal properties. Through the analysis of high-frequency drugs and drug correlation included in the prescription, we can evaluate the aetiology and pathogenesis of the disease. According to the results of the above meta-analysis, the efficacy of external traditional Chinese medicine compounds in the treatment of oral candidiasis is more accurate. Subgroup analysis shows that the disease can be effectively treated by clearing heat and

detoxification, clearing heat and purging fire, clearing heat, drying dampness and giving consideration to deficiency and excess. Further analysis of the composition of traditional Chinese medicine prescriptions shows that the occurrence of this disease is related to heat. However, more heat can change into fire. Vigorous fire can produce heat poison. The combination of dampness and heat can cause disease. Too much heat can hurt Yin fluid. Therefore, the medication group mainly focuses on clearing away heat, detoxifying or purging fire, or drying dampness or strengthening Yin, supplemented by transforming saprophytic muscles and strengthening health, to prevent excessive cold from damaging health. Thus, it provides some ideas for clinical treatment. That is, it can be dialectically applied according to the patient's condition to improve the patient's condition and treat the disease. Under the theoretical system of traditional Chinese medicine treatment, it seems undesirable to talk about medication without symptoms, but considering the main pathogenesis and object pathogenesis of disease, how can the method of summarizing effective prescriptions and commonly used high-frequency drugs not be a way to treat diseases and study the main pathogenesis of diseases? Furthermore, we can explore its effectiveness and mechanism of action through relevant network pharmacological research and animal experiments.

There are still some limitations in this study. (1) The literature included in this study is published in Chinese, so there will inevitably be some reporting bias. (2) Most of the included studies did not describe whether allocation concealment and blind design were used, so the quality of the included literature was moderate. The confidence interval of some outcome indicators is wide, so the intensity of GRADE evidence is at the middle-low level. (3) Different age groups, different treatment and follow-up times, and different medications across studies will lead to some heterogeneity. (4) The observation indicators of some studies included in the study are too single, so only the total effective rate indicators are observed, and there is a lack of data collection of research indicators such as the Candida negative conversion rate and recurrence rate. (5) Although the researchers of this study reached an agreement and signed the same written agreement according to the research type, research strategy, how to formulate inclusion and exclusion criteria, and how to conduct research and analysis, they have not registered the agreement plan. (6) There were differences in prescription composition, drug compatibility and drug dose between the study and experimental groups. It is suggested that when designing clinical trials in the future, especially in clinical trials of traditional Chinese medicine, we should not only pay attention to the practicability and preciseness of research, improve the experimental design, increase the application of the double-blind method and distribution concealment but also make treatments according to syndrome differentiation and establish an evaluation system with Chinese medicine characteristics to improve the research quality and obtain higher-quality experimental studies.

5. Conclusion

Compared with Western medicine alone, external Chinese medicine has certain advantages in improving the total effective rate, increasing the negative conversion rate of Candida and reducing the recurrence rate. However, this study still has some limitations. To overcome these limitations and better serve the clinic, it is necessary to carry out more TCM clinical trials with reasonable designs, rigorous methods, standardized medications and large scales in future research.

Statement of ethics

An ethics statement is not applicable because this study is based exclusively on published literature.

Author contribution statement

Ting Li and Qing Liu: Conceived and designed the experiments; Performed the experiments; Analysed and interpreted the data; Wrote the paper.

Qiaoyu Hu: Conceived and designed the experiments; Performed the experiments; Analysed and interpreted the data.

Jiadi Yang and Nan Zhang: performed the experiments.

Na Liu: conceived and designed the experiments; performed the experiments; interpreted the data.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no competing interests.

References

[1] D.C. Gheorghe, A.G. Niculescu, A.C. Bîrcă, A.M. Grumezescu, Biomaterials for the prevention of oral candidiasis development, Pharmaceutics 13 (6) (2021) 803.
[2] Y. Song, J. He, C. He, Distribution and epidemic trend of Candida isolates from patients with oral Candidiasis, Chin J Mycol 16 (3) (2021) 166, 169+181.

[3] A.D. Alnuaimi, D. Wiesenfeld, N.M. O'Brien-Simpson, E.C. Reynolds, M.J. McCullough, Oral Candida colonization in oral cancer patients and its relationship with traditional risk factors of oral cancer: a matched case-control study, Oral Oncol. 51 (2) (Feb 2015) 139–145.
[4] C. P, Z. JL, W. Y, F.X. Xiaochuang, Powder in treating infantile thrush of heart-spleen accumulated heat type, Jilin J. Chin. Med. 40 (5) (2020) 628–630.
[5] S. BY, Treatment of thrush in infants with integrated traditional Chinese and Western Medicine, Shenzhen J. Integrated Tradit. Chin. Western Med. 4 (1998) 25.
[6] L. R, Treatment of 33 cases of thrush in children with self-made yinlian Decoction, Zhejiang J. Tradit. Chin. Med. 54 (4) (2019) 275.
[7] G. WL, Y. Y, X. YY, Observation on curative effect and safety of using bingwu power in the treatment of oral fungal infection, J. Sichuan of Tradit. Chin. Med. 37 (9) (2019) 159–161.
[8] L. XX, H. JY, Observation and nursing of self-made Hanshu Decoction in the treatment of senile oral candidiasis, Modern Digestion & Intervention 13 (1) (2008) 53–54.
[9] G. YL, Fluconazole combined with self-made traditional Chinese medicine Hanshu formula in the treatment of 30 cases of senile oral candidiasis, Zhejiang J. Integrated Tradit. Chin. Western Med. 31 (8) (2021) 757–758.
[10] F. H, L. L, Experience of treating 50 cases of infant thrush with traditional Chinese Medicine, Guizhou Medical Journal 32 (1) (2008) 62.
[11] C. J, X. XT, H. W, V, An effective analysis of treating pediatric thrush with Qingdai Xiaobai San, Clinical Journal of Chinese Medicine 9 (22) (2017) 105–107.
[12] L. GH, H. W, Clinical observation on 40 cases of oral Candida infection treated with Yunv Decoction and Wuwei disinfection drink gargle, Zhejiang Journal of Traditional Chinese Medicine 56 (6) (2021) 439.
[13] D. MF, Clinical nursing observation of Yinqiao Powder Modified gargle on oral Candida infection in patients with advanced tumor, J. Nursing and Rehabil. 16 (7) (2016-03-18 2017) 769–771.
[14] C. W, Y. Y, L. HY, X. YY, The clinical efficacy of treatment of oral and spleen-accumulating oral candida infection in AECOPD patients treated with Bingwu San, Shaanxi J. Tradit. Chin. Med. 38 (12) (2017) 1652–1654.
[15] L. QT, B. Y, L. M, J. LY, H. H, G. JH, Clinical and experimental study on fungal I II III mixture in the treatment of candidal stomatitis, pulmonary candidiasis and candidal enteritis, J. Tradit. Chin. Med. 2 (2001) 98–100.
[16] Y. JJ, Clinical observation on the efficacy of the traditional Chinese medicine "Wubai Decoction" combined with fluconazole on oral candidiasis, Shanghai J. Tradit. Chin. Med. 49 (7) (2015) 53–55.
[17] S. ZJ, Effect of external application of traditional Chinese medicine on thrush in infants, Inner Mongolia J. Tradit. Chin. Med. 39 (4) (2020) 51–52.
[18] S. HY, Clinical observation on the treatment of infant thrush by external use of Chinese medicine, J. Pract. Stomatology 31 (1) (2015) 125–126.
[19] Y. K, Clinical observation of integrated traditional Chinese and Western medicine in the treatment of senile oral candidiasis, China Rural Health 6 (2017) 25.
[20] Z. HW, J. HY, Z. JY, Treatment of 32 cases of thrush with integrated traditional Chinese and Western Medicine, Modern J. Integrated Tradit. Chin. Western Med. 16 (16) (2007) 2263–2264.
[21] L. WF, L. B, Self-made Chinese medicine gargle combined with itraconazole for treating denture stomatitis in 31 cases, China Pharmaceut. 24 (19) (2015) 109–110.
[22] R. C, Wubai decoction combined with fluconazole in the treatment of oral candidiasis for 50 cases, Chin. Med. Modern Distance Educ. China 13 (23) (2015) 60–61.
[23] Z. ZL, C. TX, 126 cases of thrush in children treated with Qingmei powder, J. Zhejiang Chin. Med. University 22 (3) (1998) 27.
[24] W. CY, Clinical observation on 50 cases of Oral Candidiasis of spleen deficiency damp heat type treated with Huanglian and Wubai powder, Zhejiang J. Tradit. Chin. Med. 54 (8) (2019) 587–588.
[25] P. Y, Z. LQ, S. P, External application of Han Dai powder combined with fluconazole in the treatment of 35 cases of Oral Candidiasis, Tradit. Chin. Med. Res. 30 (1) (2017) 25–27.
[26] N. WL, Treatment of 132 cases of thrush with ejouchuang powder, J. External Therapy Tradit. Chin. Med. 22 (5) (2013) 62.
[27] Y. LY, Clinical study on shenxian shukou liquid combined with itraconazole for treating intractable oral candidiasis, Acta Chinese Medicine 26 (10) (2011) 1260–1261.
[28] X. YY, Y. Y, Bingwu powder on secondary oral candidiasis infection of COPD, J. Changchun University of Chin. Med. 34 (1) (2018) 136–138.
[29] L. X, G. GY, 60 cases of thrush treated by external application of traditional Chinese Medicine, Cont. Med. Educ. 27 (12) (2013) 23.
[30] C. Z, Analysis of the efficacy of topical use of traditional Chinese medicine in the treatment of thrush in infants and young children, Women's and Children's Health Guide 11 (10) (2021) 30–31.
[31] K. GY, Clinical effect of sore-elimination powder treatment of thrush in infants and young children with cardiosplenic fever, Women's and Children's Health Guide 11 (9) (2021) 27–28.
[32] L. L, C. YX, X. JH, L. DC, Clinical observation of Jinpu with gargle in the treatment of candidal stomatitis, Med. Theory Pract. 34 (20) (2021) 3583–3585.
[33] T.S. Zhang, S.X. Zhang, How to compare summary estimates of different subgroups in meta-analysis, Chin. J. Evidence-Based Med. 17 (12) (2017) 1465–1470.
[34] P.H. Wu, T. Xie, H.Y. Wang, R.Q. Fan, In vitro experimental study on the synergism of Coptis decoction against Candida, Chin. J. Dermatovenereol. Integrat. Tradit. Western Med. 19 (3) (2020) 205–210+215.
[35] Y.Y. Zhao, Y.H. Guo, S.M. Huang, B.Q. Yin, Y.P. Tang, Advances in research on the pharmacological effects and molecular mechanisms of Borneol guiding action, J.Nanjing University of Tradit. Chin. Med. 37 (1) (2021) 150–155.