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REVIEW ARTICLE

A Systematic Review and Meta-Analysis of the Role of *Prosopis cineraria* in the Treatment of Non-Communicable Diseases (NCDs)

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Abstract

Non-communicable diseases (NCDs) are chronic long-lasting disorders spreading worldwide. *Prosopis cineraria* as an Indian herbal plant possess pharmacological activities used in treating varied NCDs. However, a systematic review of *Prosopis cineraria* and its therapeutic properties in treating NCDs is still not available. So, to determine the adequacy of *Prosopis cineraria* in treating NCDs, a systematic meta-interpretive literature review was accomplished in this current paper in which 106 research papers on *Prosopis cineraria* were retrieved from the databases. Out of 106 studies, meta-analysis was performed by using MedCalc – version 20.116 on studies retrieved from 22 publications that projected *Prosopis cineraria* as an Indian herbal plant used for traditional NCDs treatment. 11 studies out of 22 show effective results in treating NCDs by using *Prosopis cineraria* as an herbal medicine. In these studies, the *in vitro* research was preferred as they include primary outcomes of research to further proceed for *in vivo* research. The plant part and solvent usage pattern of *Prosopis cineraria* showed variability across the *in vitro* and *in vivo* designs of the studies. By meta-analysis on *Prosopis cineraria* as a folk medication indicated that mainly leaves and stem bark extracted by using ethanol, methanol, petroleum ether, butanol, ethyl acetate, and aqueous solvents were used as they contain bioactive constituents showing antidiabetic, anticancer, anti-inflammatory, antioxidant, antimicrobial, antihyperlipidemic potentials to treat NCDs also giving highly effective prediction ideas through computational biology.

Keywords: Indian drugs, *in vitro* and *in vivo* analysis, non-communicable diseases, *Prosopis cineraria*.

Introduction

Non-communicable diseases (NCDs) are chronic non-infectious progressively long-lasting disorders. They are mainly distinguished by diabetes, cancer, cardiovascular, and pulmonary diseases (Nethan *et al.*, 2017). According to the World Health Organization report, NCDs are the cause of death and their health sector costs of diseases were predicted to be about 6% of the total healthcare budget, in which 74% of the total death cases were reported (World Health Organization, 2011). A prediction on risk factors of NCDs will rise by 2030 as evaluated by Yang Wang in his study (Wang and Wang, 2020). Though the use of western medicines is effective in controlling and treating a group of NCDs, they may also have several side effects (Al-Saadoon, 2015). To reduce these harmful effects the usage of herbal remedies are widely perceived as natural and safe as they are rich in a variety of compounds in the form of secondary metabolites including aromatic substances most of which are phenols and flavonoids having antioxidant properties (Jangid *et al.*, 2022). One such plant widely used for treating various lifestyle disorders is *Prosopis cineraria.* Several studies have shown the therapeutic role of *Prosopis cineraria* as a medicinal plant in recovering NCDs by using different parts of the herb and solvents in *in-vitro* and *in-vivo* types of research studies (Janbaz *et al.*, 2012).

Prosopis cineraria, locally named "Khejri" or "Shami" tree in India, belongs to the family Leguminosae. It is a multipurpose endemic tree commonly available in the hot deserts of Rajasthan, India (Chaudhary *et al.*, 2018). Almost every part of this plant has effectively been used since ancient times particularly for multipurpose benefits, as it contains several essential phytochemicals, and bioactive constituents as secondary metabolites that demonstrate various biological functions such as antidiabetic, anticancer, antimicrobial, analgesic, anthelmintic, antibiotic, antiemetic, antioxidant, antimalarial, anti-protozoan, anti-pustule, and antiulcer activities (Jangid *et al.*, 2022). The antioxidant,

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antidiabetic, antimicrobial, and anticancer potentials have been considered the gold standard in treating NCDs.

Antioxidant compounds inhibit the imbalance production of reactive oxygen species and oxidative stress caused by cellular damage. Several studies reported that *Prosopis cineraria* is a herbal supplement with antioxidant potential, and eliminates oxidative stress development as it contains several bioactive constituents rich in phenols and flavonoids (Mohammad *et al.*, 2013). Several researchers concluded that ethanolic, methanolic, ethyl acetate, and chloroform extracts of stem bark and a leaf of *Prosopis cineraria* exhibit antioxidant potential (Choudhary *et al.*, 2011; Mohammad *et al.*, 2013; Soni *et al.*, 2015).

The antidiabetic role of *Prosopis cineraria* in lowering the high blood glucose level was reported in several studies. Sharma (2010) and Soni (2018) with their research team stated about the antihyperglycemic potential of ethanolic and chloroform bark extracts of *Prosopis cineraria* in male mice injected with alloxan and STZ, respectively (Sharma *et al.*, 2010; Soni *et al.*, 2018). Sharma in 2013 reported that the hydroalcoholic leaf extract of *Prosopis cineraria* is also effective in lowering the high blood glucose level (Sharma and Singla, 2013). The ethyl acetate and n-butanol pod extract of *Prosopis cineraria* are effective in inhibiting the level of alpha-glucosidase and alpha-amylase, respectively as concluded by Kumar, 2019 (Kumar *et al.*, 2019).

The presence of secondary metabolites such as flavonoids and phenolic compounds in *Prosopis cineraria* possesses antimicrobial and antibacterial potential thus inhibiting microbial growth and reducing microorganism infections. Preeti and group stated in their findings that by conducting the agar well diffusion method the leaf, stem, and pod parts of *Prosopis cineraria* show antimicrobial activities (Preeti *et al.*, 2017).

The anticancer potential of the stem bark of *Prosopis cineraria* was responsible for inhibiting the cancer risk as reported by Robertson and Narayanan (Robertson and Narayanan, 2014). In a research finding it was concluded that the ethanolic stem bark of *Prosopis cineraria* shows anticancer potential (Robertson *et al.*, 2011). In a study, the effective anticancer role of the methanolic leaf extract of *Prosopis cineraria* was carried on by inhibiting cell proliferation against breast cancer cell line (Sundaravadivelu S., 2012).

In this current paper, we systematically reviewed the effectiveness of *the Prosopis cineraria* plant in treating NCDs via its antioxidant, anticancer, and antidiabetic functions as the primary outcomes. It also shows positive outcomes on several other therapeutic functions and is considered cost-effective. In addition, the commonly used plant parts and solvents for *Prosopis cineraria* extract preparation, the study type, and several pharmacological activities of the herbal plant were analyzed for treating NCDs.

Methodology

Literature search and databases

For the study following search engines were used - PubMed; Google Scholar; Elsevier bio base; EMBASE; Web of Science; and ScienceDirect. The keywords search was conducted in January 2022 and updated in November 2022, including the following terms: "Indian drugs", "Traditional Indian medicine" "Indian herbal supplements", "Indian herbal tablet", "herbal formulation", "Folk herbal medicines", "Home herbal remedies", "herb", "Indian medicinal plant", "medicinal herbal product", "plant extraction preparation", "Herb therapy", "Herbal therapy", "unconventional medicine", "complementary herbal therapy", "Non-Communicable diseases or (NCDs)", "diabetes mellitus (DM)", "type 2 diabetes", "antioxidant", "anticancer", "*Prosopis cineraria*", "antihyperglycemic", "antihyperlipidemic", "analgesic", "antibacterial", "antipyretic", "anti-inflammatory", "antispasmodic", "nanoparticles", "wound healing", "fertility", "bronchodilator", "vasodilator", "anti-diarrhoeal", "enzyme inhibition", "lipid peroxidation". Additional research was identified by manual searching of references in original articles and review articles.

Inclusion and Exclusion Criteria

The preference was given to the most significant and reviewed articles and abstracts of all published research papers reporting randomized controlled trials (RCTs) on *Prosopis cineraria* as herbal medicine. All the chosen studies included the following measures: (a) publication in English, (b) data that helps to calculate the odds ratio for *Prosopis cineraria*, (c) analysis of case-control studies which included the correlation between different types of tests and treatments for diagnosis and evaluate the risk factors of NCD, (d) when numerous publications were present on the same data or overlying data, the best or most recent publication was selected. The major exclusion criteria were as follows: (a) papers characterized as reviews, abstracts, or case reports, (b) unpublished papers and reports, and (c) meta-analysis already done on case-control group studies. The research interventions on *Prosopis cineraria* could include either (1) plant extract preparation by using different parts of

the plant; (2) intervention groups with herbal treatments; or (3) different therapeutic properties of an herbal product(s). The prepared plant extract should be administered alone or in combination with allopathic medicines. The time duration of the research experiment had no limitations in acceptance. Both *in vivo* and *in vitro* analyses were accepted. The antioxidant, anticancer, antidiabetic, and all other necessary pharmacological or therapeutic roles of *Prosopis cineraria* in the research studies had to be reported for acceptance for further meta-analysis. Studies were excluded during clinical trials without baseline and endpoint of antioxidant, anticancer, antidiabetic functions, and other medical properties of the herbal plant.

Statistical analysis

The analysis of 22 studies was performed using freely available MedCalc – 20.116 software. The mean difference (MD), 95% confidence interval (CI), and forest plot were assessed for measuring primary outcome variables. To evaluate the strength of the analysis, random and fixed effect heterogeneity (I^2) was employed in which a value of I^2 greater than 50% shows Random Heterogeneity and a value of I^2 smaller than 50% shows Fix effect Heterogeneity model. For subgroup analysis, the continuous and dichotomous outcome variables with a 95% (CI) and odds ratio (OR) were also employed based on different medical values of the plant. The statistically significant assessment was evaluated to study the combined effects between the intervention and the control groups.

Results and Discussion

Characterization of studies

Abstracts of 106 published papers were monitored and retrieved from online databases, out of which, 55 were rejected because of irrelevant and insufficient data while 28 full research papers were included for further investigation. Thereafter, 22 studies that satisfied the relevant criteria on *Prosopis cineraria* were meta-analyzed for their possible role in treating NCDs as shown in Fig. 1. The main characteristics of 22 high-quality fully relevant research studies for meta-analysis are shown in Table 1.

To identify the commonly evaluated plant pharmacological activities for treating NCDs, we counted the frequency of treatments based on different solvents and parts of *Prosopis cineraria* used to extract phenolic and flavonoid compounds as secondary metabolites from the medicinal plants that were utilized in the 22 clinical trials. Common therapeutic properties of *Prosopis cineraria* in treating NCDs were mentioned in Fig. 2. The antioxidant, anticancer activity and tests for detecting organ toxicity in antidiabetic activity were mostly preferred for both *in vitro* and *in vivo* studies in evaluating the therapeutic role of herbal medicine. To further confirm the findings, 22 clinical studies were identified in which the most frequently used treatments were analyzed and compared. In addition to this, some routine tests such as antibacterial, antimicrobial, and microbial overload were commonly favored in ameliorating NCDs. Specifically, antidiabetic and

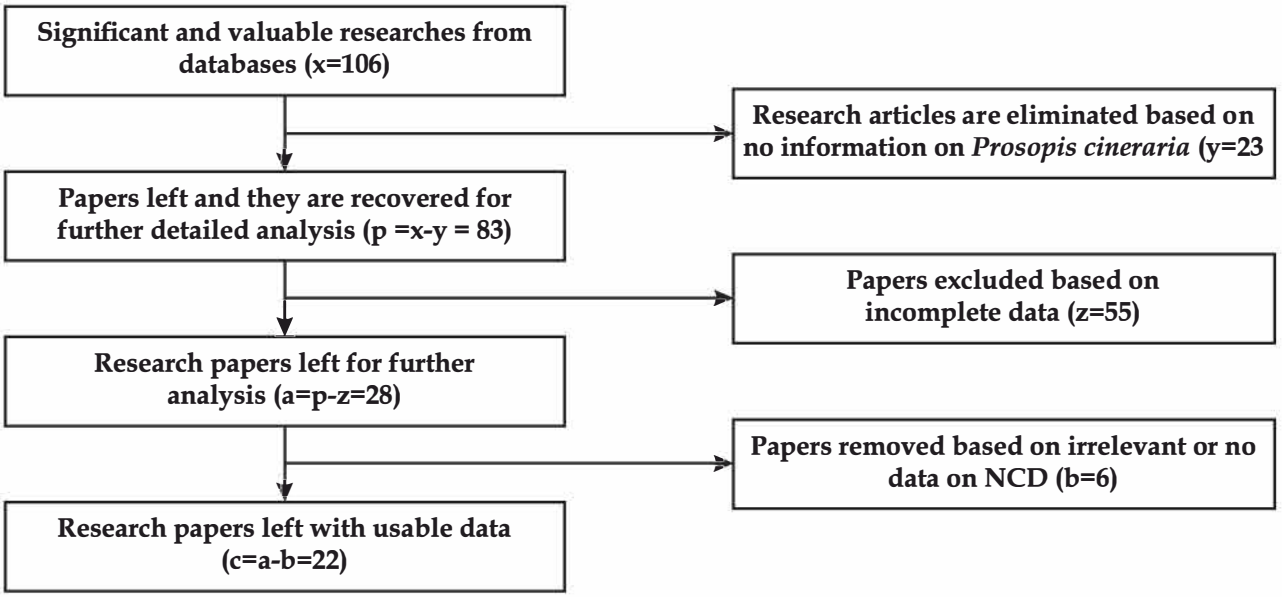

Fig. 1. The flow chart of studies that satisfied the relevant criteria on *Prosopis cineraria* for meta-analysis.

Table 1: Main characteristics of studies included in the meta-analysis

S.No.	Study groups	Design	Plant part	Plant solvent	Diagnosis	Assays/Tests conducted
1.	Jangid *et al.*, 2022	*in vitro*	Stem bark	Ethanol	Phytochemicals Antioxidant In vitro antidiabetic	Total phenolic content Total flavonoid content DPPH FRAP alpha amylase - DNSA method
2.	Asati, *et al.*, 2021	*in vitro*	Pods	Methanol	Antioxidant Anticancer	DPPH In vitro cytotoxicity assay Bright field imaging and dye exclusion assay Flow cytometric analysis of apoptotic cells
3.	Ram, *et al.*, 200	*in vitro/in vivo*	Pods	Ethanol	Hypercholesterolemia Antihyperlipidemic Antioxidant Molecular docking	in vitro HMG-CoA reductase inhibition Serum lipid profile Antioxidant properties Molecular docking
4.	Ramalingam *et al.*, 2020	*in vivo*	Pods	Hydroalcoholic	Male fertility	Body weight Reproductive organ weight Hormones Epididymal sperm count Sperm motility, viability, density, morphology Membrane stability test Testicular sperm head count Sperm production per gram testis Antioxidant parameters
5.	Sharma and Sharma, 2020	*in vivo*	Stem bark	Hydroethanol	Anti-inflammatory	Cytokine levels study Nitric oxide level study NF-kBp65 level study
6.	Sharma *et al.*, 2020	*in vitro*	Stem bark	Petroleum ether, chloroform,ethyl acetate, ethanol, hydroethanol, aqueous	Antioxidant	Secondary metabolites analyzed Antioxidant activity
7.	Nodushan *et al.*, 2020	*in vivo*	Stem bark	Ethanol	Atopic dermatitis	Atopic Dermatitis
8.	Kumar *et al.*, 2019	*in vitro/ in vivo*	Pods	Ethyl acetate	Phytochemicals Anti-diabetic	total phenolic content total flavonoid content
9.	Soni *et al.*, 2018	*in vivo /in vitro*	Stem bark	Chloroform	Antidiabetic Antihyperlipidemic In vitro antidiabetic	Blood glucose level Body weight HbA1C Insulin level Serum lipid profile Total glycogen content alpha amylase antidiabetic activity

S.No.	Study groups	Design	Plant part	Plant solvent	Diagnosis	Assays/Tests conducted
10.	Yadav *et al.,* 2018	*in vitro/in vivo*	Leaf	Butanol	Antioxidant Phytochemicals Enzyme inhibition Wound healing Antioxidant Anti-inflammatory	ABTS estimation of phenolic compounds albumin denaturation Proteinase inhibitor activity collagenase inhibitory activity elastase inhibitory activity excision wound activity antioxidant parameters inflammatory markers
11.	Jinu *et al.,* 2017	*in vitro*	Leaf	Nanoparticles	Antimicrobial Anticancer	Antibacterial activity - disc method In vitro cytotoxicity determination by MTT assay Acridine orange (AO) and ethidium bromide (EtBr) staining assay DNA fragmentation analysis
12.	Satish *et al.,* 2015	*in vitro*	Pods	Ethyl acetate	antimalarial	in vitro antimalarial screening Cytotoxicity of extracts on THP -1 monocyte cell line
13.	Jain *et al.,* 2015	*in vitro/ in vivo*	Pods	Ethanol	Antioxidant Antihyperlipidemic Molecular docking	DPPH Serum lipid profile Molecular docking
14.	Sharma *et al.,* 2013	*in vivo*	Leaf	Hydroalcoholic	Antidiabetic Antihyperlipidemic	Blood glucose level Body weight Serum lipid profile
15.	Pakkir Maideen *et al.,* 2012	*in vivo*	Leaf	Methanol	Anticancer	Membrane ATPase activities glycoproteins
16.	Janbaz *et al.,* 2012	*in vivo*	Stem bark	Methanol	Antispasmodic Bronchodilator Vasodilator	Antispasmodic Activity on Jejunum, Ca+2 Channel Blocking Activity Bronchodilator Activity on Tracheal Vasodilator Activity on Aorta
17.	Deshavath *et al.,* 2012	*in vivo*	Stem bark	Methanol	Antidiarrhoeal	Antidiarrhoeal activity Gastrointestinal motility
18.	Liu *et al.,* 2012	*in vitro*	Pods	Methanol	Antioxidant Enzyme inhibition	MTT assay Lipid peroxidation inhibitory assay COX-1 and -2 enzymes inhibitory assay
19.	Khatri *et al.,*2011	*in vivo*	Stem bark	Petroleum ether, methanolic and aqueous	Anthelminthic	Anthelmintic activity
20.	Velmurugan *et al.,* 2011	*in vivo*	Stem bark	Methanol	Anthelmintic	Anthelmintic activity
21.	Sharma *et al.,* 2010	*in vivo*	Bark	Hydroalcoholic	Antidiabetic Antihyperlipidemic Antioxidative	Blood glucose level Body weight Total glycogen content Serum lipid profile Antioxidative status
22.	Manikandar *et al.,* 2009	*in vivo*	Stem bark	Petroleum ether, ethyl acetate, ethanol	Analgesic Antipyretic	Eddy's hot plate method Brewer's yeast induced hyperpyrexia method

anticancer were among the frequently used tests for antihyperglycemic studies, they all overlapped in NCD treatment, which was further confirmed in the meta-analysis interpretation as shown in Fig. 2.

CI and OR values

For Meta-analysis 22 studies consisting of intervention and case-control groups on the basis of inclusion criteria were considered. The features are arranged in Table 2. In these studies, research work on *Prosopis cineraria* consisted of activities viz. antioxidants (10), anticancer (3), antidiabetic (6), antihyperlipidemic (5), and anthelmintic (2). Then based on the characterization of different groups and subgroups 21 types of *in vitro* and *in vivo* assays were used among which DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate), *in vitro* cytotoxicity assay, fasting blood glucose level and serum biochemical parameter tests for treating NCDs were mostly preferred.

The meta-analysis for the included 22 studies reported that *Prosopis cineraria* as an herbal medicine showed an advantage in treating NCDs in 11 studies (total effect P = 0.3364, I_2= 9.26%) mentioned in Table 3 (a and b). While rest 11 studies showed no advantage of using *Prosopis cineraria* in treating NCDs as they favor the control side of baseline which shows no significant difference as shown in Fig. 3.

Next, a meta-analysis was conducted for different parts of the plant used to prepare the extracts for research use as they contain several secondary metabolites as bioactive constituents. The result reported that the leaves and stem bark of *Prosopis cineraria* is more effective in treating the NCD as they favor the experimental side of the baseline as shown in Fig. 4. (Overall effect P = < 0.0001, heterogeneity I_2= 98.91%) mentioned in Table 4 (a and b).

The meta-analysis on the use of solvents in extract preparation clearly shows ethanol, methanol, ethyl acetate, petroleum ether, butanol, and aqueous solvents

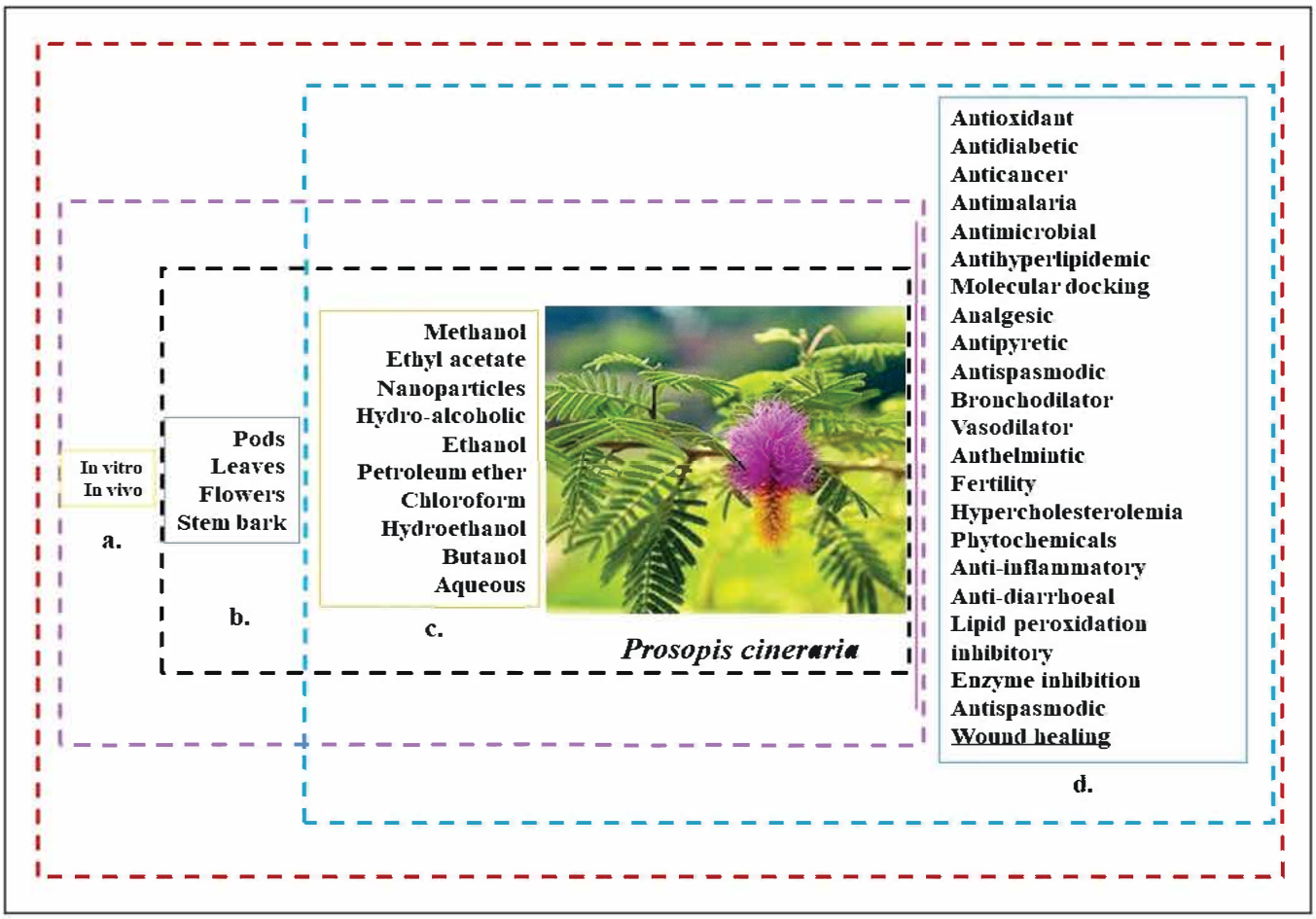

Fig. 2. The four groups and subgroups of *Prosopis cineraria* overlapped in NCD. (a.) the design of the study, (b.) different parts of the plant, (c.) different solvents used in plant extract preparation, (d.) different assays/tests conducted.

Table 2: Distribution of cases and controls in the studies of *Prosopis cineraria* included in the meta-analysis

Comparison	No. of studies	Sample size	Intervention group		Control group	
			Cases	Positive outcomes	Controls	Positive outcomes
Parts						
Total	**22**	**4727/1535**	**2658**	**2069**	**900**	**635**
Leaf	4	913/310	557	356	160	150
Pod	7	1640/435	915	725	340	95
Stem bark	11	2165/783	1180	985	394	389
Flowers	1	9/7	6	3	6	1
Solvents						
Total	**22**	**5208/1815**	**3810**	**1398**	**1104**	**711**
Ethanol	6	450/150	300	150	78	72
Methanol	7	320/126	213	107	66	60
Ethyl acetate	4	443/138	354	89	72	66
Petroleum ether	3	954/327	715	239	202	125
Hydroalcoholic	2	892/303	595	297	203	100
Nanoparticles	1	228/60	152	76	40	20
Hydro-ethanol	2	323/54	216	107	36	18
Chloroform	2	574/135	383	191	95	40
Butanol	1	745/326	638	107	211	115
Aqueous	1	276/196	244	35	101	95
Research methods						
Total	**22**	**4283/2194**	2660	1623	1178	1016
Antioxidant	10	**1353/529**	785	568	293	236
Anticancer	3	**173/89**	98	75	43	40
Antidiabetic	6	**456/550**	281	175	284	266
Antimicrobial	1	**147/33**	90	57	18	15
Antimalaria	1	**9/9**	6	3	6	3
Molecular docking	2	**5/3**	4	1	2	1
Antihyperlipidemic	5	**516/265**	360	156	135	130
Fertility	1	**741/244**	373	368	124	120
Antipyretic	1	**24/9**	18	6	6	3
Analgesic	1	**24/9**	18	6	6	3
Bronchodilator	1	**8/3**	5	3	2	1
Vasodilator	1	**8/3**	5	3	2	1
Anthelmintic	2	**17/6**	13	4	4	2
Hypercholesterolemia	1	**6/6**	5	1	5	1
Phytochemicals	4	**300/58**	228	72	30	28
Anti-inflammatory	4	**220/250**	144	76	130	120
Anti-diarrhoeal	1	**40/17**	30	10	10	7
Lipid peroxidation inhibitory	1	**40/18**	36	4	12	6
Enzyme inhibition	2	**116/69**	102	14	46	23
Antispasmodic	1	**8/3**	5	3	2	1
Wound healing	1	**72/27**	54	18	18	9
Design						
Total	**22**	**3203/1269**	2556	647	945	324
***in vitro* study**	11	**1110/416**	952	158	291	125
***in vivo* study**	16	**2093/853**	1604	489	654	199

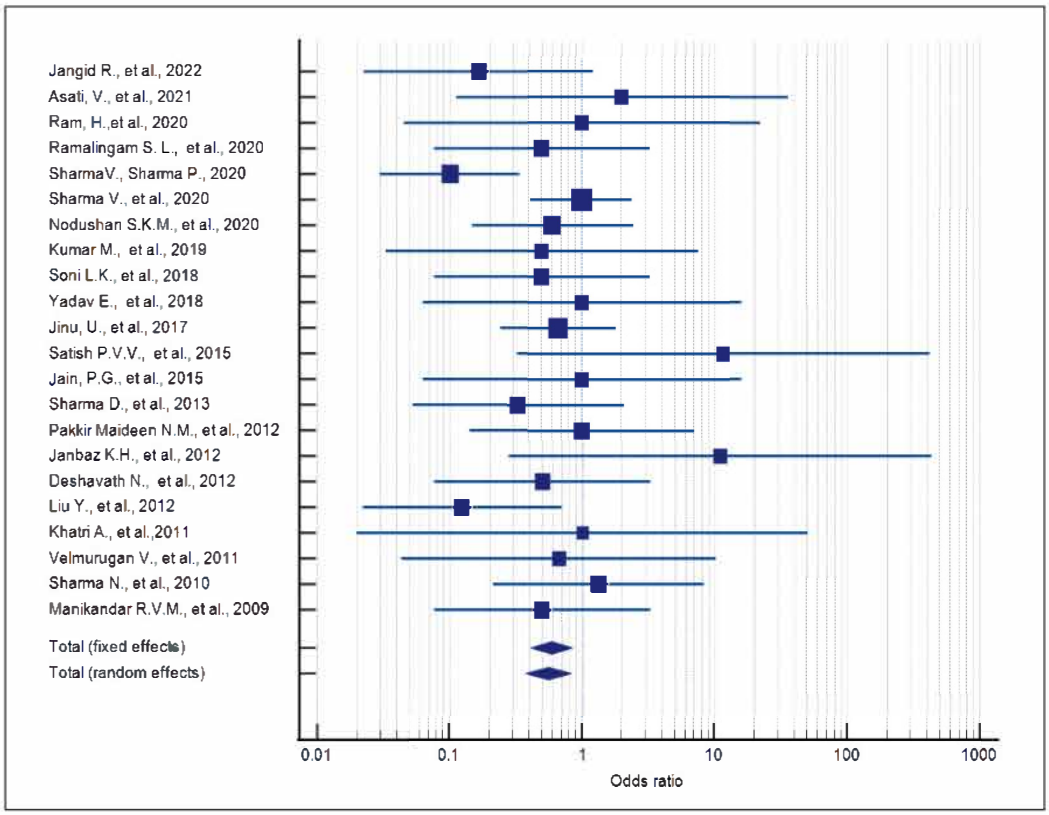

Fig.3 Meta-analysis of studies on *Prosopis cineraria* for treating NCDs.

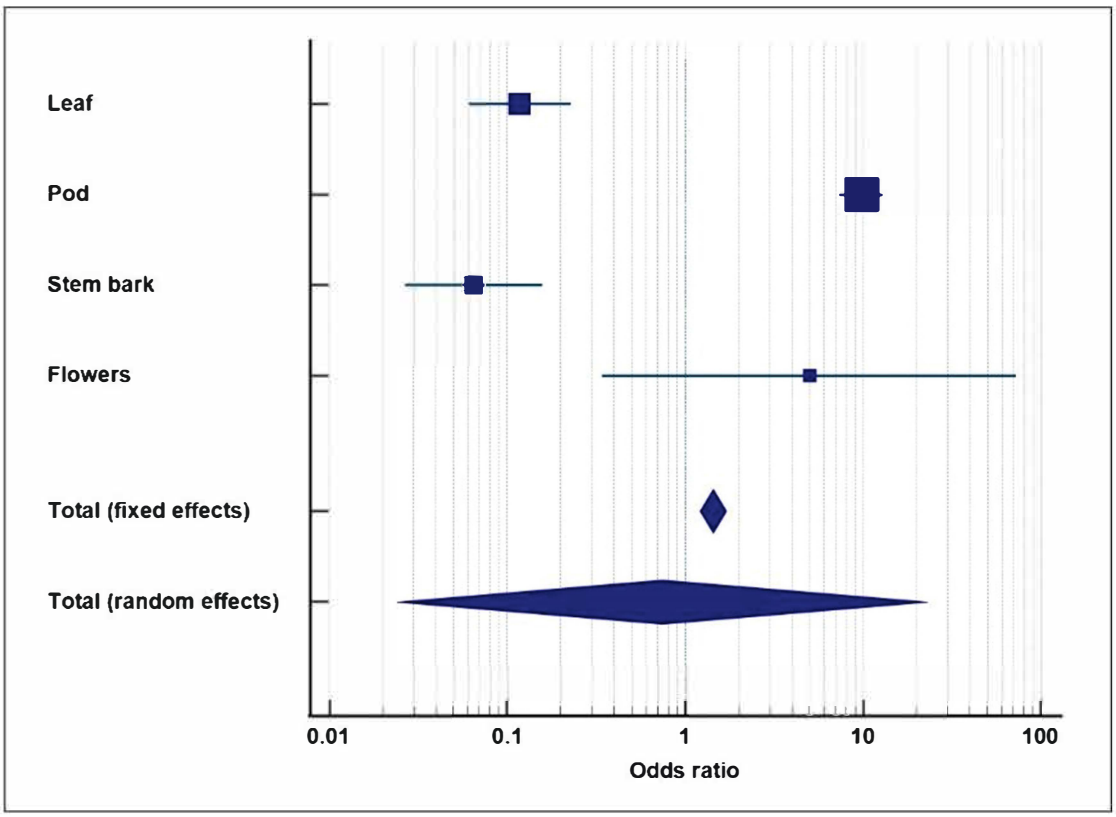

Fig. 4. Meta-analysis of parts used for *Prosopis cineraria* extract preparation.

in descending order of preference as they are supporting the experiment side baseline in Fig. 5 (overall effect P = < 0.0001, heterogeneity I_2 =95.97%) and mentioned in Table 5 (a and b).

A meta-analysis for modalities of *Prosopis cineraria* in the treatment of NCD disorders shows antidiabetic, anticancer, antioxidant, antimicrobial, *in silico*, antihyperlipidemic, anti-inflammatory properties of the

Table 3 (a). Results of a meta-analysis of studies on *Prosopis cineraria* for treating NCDs

Study	Intervention	Controls	Odds ratio	95% CI	z	P	Weight (%)	
							Fixed	Random
Jangid *et al*., 2022	6/30	3/5	0.167	0.0225 to 1.232			3.57	3.76
Asati *et al*., 2021	3/6	1/3	2.000	0.112 to 35.809			1.72	1.85
Ram *et al*., 2020	1/5	1/5	1.000	0.0451 to 22.176			1.49	1.61
Ramalingam *et al*., 2020	6/18	3/6	0.500	0.0766 to 3.265			4.06	4.25
Sharma and Sharma, 2020	15/90	10/15	0.100	0.0299 to 0.335			9.78	9.61
Sharma *et al*., 2020	30/60	15/30	1.000	0.416 to 2.403			18.59	16.64
Nodushan *et al*., 2020	6/16	8/16	0.600	0.147 to 2.455			7.19	7.28
Kumar *et al*., 2019	3/15	1/3	0.500	0.0332 to 7.541			1.94	2.09
Soni *et al*., 2018	6/18	3/6	0.500	0.0766 to 3.265			4.06	4.25
Yadav *et al*., 2018	3/9	1/3	1.000	0.0625 to 15.988			1.86	2.00
Jinu, *et al*., 2017	36/90	9/18	0.667	0.241 to 1.841			13.84	13.02
Satish *et al*., 2015	3/3	1/3	11.667	0.322 to 422.166			1.11	1.20
Jain, *et al*., 2015	3/9	1/3	1.000	0.0625 to 15.988			1.86	2.00
Sharma *et al*., 2013	6/24	3/6	0.333	0.0525 to 2.116			4.18	4.38
Pakkir Maideen *et al*., 2012	6/12	3/6	1.000	0.141 to 7.099			3.72	3.91
Janbaz *et al*., 2012	5/5	1/2	11.000	0.279 to 433.828			1.06	1.15
Deshavath *et al*., 2012	6/18	3/6	0.500	0.0766 to 3.265			4.06	4.25
Liu *et al*., 2012	4/36	4/8	0.125	0.0221 to 0.707			4.76	4.95
Khatri *et al*.,2011	1/2	1/2	1.000	0.0198 to 50.400			0.93	1.01
Velmurugan *et al*., 2011	3/12	1/3	0.667	0.0433 to 10.254			1.91	2.06
Sharma *et al*., 2010	7/14	3/7	1.333	0.214 to 8.288			4.28	4.47
Manikandar *et al*., 2009	6/18	3/6	0.500	0.0766 to 3.265			4.06	4.25
Total (fixed eff ects)	165/510	79/162	0.587	0.408 to 0.844	-2.872	0.004	100.00	100.00
Total (random effects)	165/510	79/162	0.556	0.374 to 0.826	-2.904	0.004	100.00	100.00

Table 3 (b). Test for heterogeneity and Publication bias of studies on *Prosopis cineraria* for treating NCDs

Heterogeneity	
Q	22.1307
DF	21
Significance level	P = 0.3920
I^2 (inconsistency)	5.11%
95% CI for I^2	0.00 to 37.12

Publication bias	
Egger's test	
Intercept	0.6568
95% CI	-0.4846 to 1.7982
Significance level	P = 0.2440
Begg's test	
Kendall's Tau	0.3304
Significance level	P = 0.0314

Table 4 (a). Result of Meta-analysis of parts used for *Prosopis cineraria* extract preparation.

Study	Intervention	Controls	Odds ratio	95% CI	z	P	Weight (%)	
							Fixed	Random
Leaf	356/557	150/160	0.118	0.0608 to 0.229			14.29	25.83
Pod	725/915	95/340	9.841	7.395 to 13.095			76.99	26.04
Stem bark	985/1180	389/394	0.0649	0.0265 to 0.159			7.84	25.63
Flowers	3/6	1/6	5.000	0.344 to 72.770			0.88	22.50
Total (fixed effects)	2069/2658	635/900	1.439	1.213 to 1.706	4.184	<0.001	100.00	100.00
Total (random effects)	2069/2658	635/900	0.744	0.0242 to 22.883	-0.169	0.866	100.00	100.00

Table 4 (b). Test for heterogeneity and Publication bias of parts used for *Prosopis cineraria* extract preparation

Heterogeneity	
Q	275.4215
DF	3
Significancelevel	P < 0.0001
I^2 (inconsistency)	98.91%
95% CI for $\hat{I}$	98.35 to 99.28

Publication bias	
Egger'stest	
Intercept	-8.4836
95% CI	-38.3866 to 21.4195
Significancelevel	P = 0.3466
Begg'stest	
Kendall'sTau	0.0000
Significancelevel	P = 1.0000

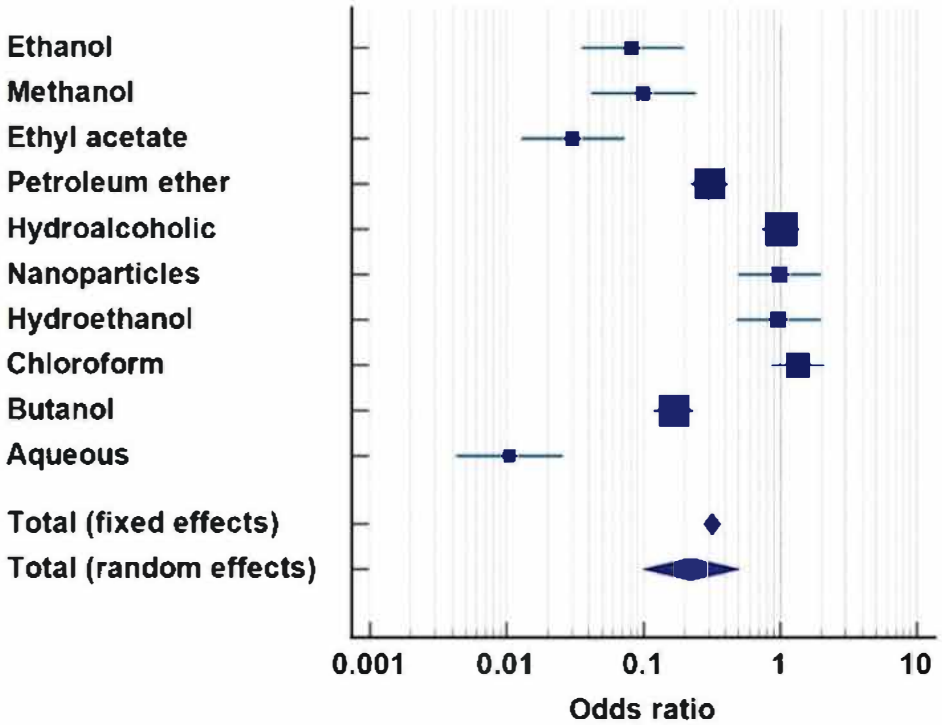

Fig. 5. Meta-analysis of solvents in treating NCD with *Prosopis cineraria*

Table 5 (a). Result of Meta-analysis of solvents in treating NCD with Prosopis cineraria.

Study	Intervention	Controls	Odds ratio	95% CI	z	P	Weight (%)	
							Fixed	Random
Ethanol	150/300	72/78	0.0833	0.0352 to 0.198			3.19	9.57
Methanol	107/213	60/66	0.101	0.0418 to 0.244			3.06	9.52
Ethyl acetate	89/354	66/72	0.0305	0.0128 to 0.0728			3.14	9.55
Petroleum ether	239/715	125/202	0.309	0.224 to 0.428			22.68	10.55
Hydroalcoholic	297/595	100/203	1.027	0.746 to 1.412			23.40	10.55
Nanoparticles	76/152	20/40	1.000	0.498 to 2.007			4.90	9.94
Hydro-ethanol	107/216	18/36	0.982	0.485 to 1.988			4.77	9.92
Chloroform	191/383	40/95	1.368	0.869 to 2.154			11.53	10.38
Butanol	107/638	115/211	0.168	0.120 to 0.237			20.39	10.53
Aqueous	35/244	95/101	0.0106	0.00430 to 0.0260			2.94	9.48
Total (fixed effects)	1398/3810	711/1104	0.322	0.280 to 0.370	-15.971	<0.001	100.00	100.00
Total (random effects)	1398/3810	711/1104	0.223	0.0993 to 0.503	-3.621	<0.001	100.00	100.00

Table 5 (b). Test for heterogeneity and Publication bias of solvents in treating NCD with *Prosopis cineraria.*

Heterogeneity	
Q	223.2796
DF	9
Significance level	P < 0.0001
I^2 (inconsistency)	95.97%
95% CI for I^2	94.16 to 97.22

Publication bias	
Egger'stest	
Intercept	-5.1017
95% CI	-13.5990 to 3.3955
Significancdevel	P = 0.2036
Begg'stest	
Kendall'sTau	-0.5556
Significancdevel	P = 0.0253

plant favor the experiment side baseline in Fig. 6 (Overall effect P= < 0.0001, heterogeneity I_2=79.70%) and Table 6 (a and b).

Lastly to analyze the design/type of studies, *in vitro* studies were reported to be more preferred in showing *Prosopis cineraria* as an effective therapeutic agent as the studies include all the primary outcomes of the research which further allows the investigator to perform *in vivo* analysis as shown in Fig. 7 (overall effect P = P < 0.0001, heterogeneity I_2= 98.22%) and Table 7 (a and b).

The growing burden of NCDs (cancer, diabetes, cardiovascular, and pulmonary diseases) cause morbidity and mortality worldwide (Wachtel-Galor and Benzie., 2011). Knowing the therapeutic potential of herbal medicines is the essential criterion for treating NCDs several research papers on *Prosopis cineraria* have shown the therapeutic potential of different plant parts/extracts in treating NCDs but no systematic literature review was published. Due to this reason, our current review provides an updated literature survey on the adequacy of *Prosopis cineraria* as herbal medicine as it is more affordable, closely corresponds to the patient's ideology, and allows greater public access to health information. The treatment of NCDs using different

parts of the plant used, solvent used in extract preparation, and designs of the study are the primary outcomes of this review. Many studies claimed improvement in treatment after combining it with *Prosopis cineraria* intake. Interestingly, the antidiabetic endpoints like blood glucose level and bodyweight measurements showed a role in controlling type 2 diabetes complications, but it remains unresolved due to varied diversity among the research studies. On the contrary, the bronchodilator and vasodilator parameters associated with cardiovascular disease treatment are not found significant while administering *Prosopis cineraria* so the irrelevance of data excludes these research papers for meta-analysis. For extract preparation, parts of the plant and the solvents are considered the primary outcome in treating NCDs. The anticancer properties of *Prosopis cineraria* showed an effective improvement compared to traditional treatment modalities in many

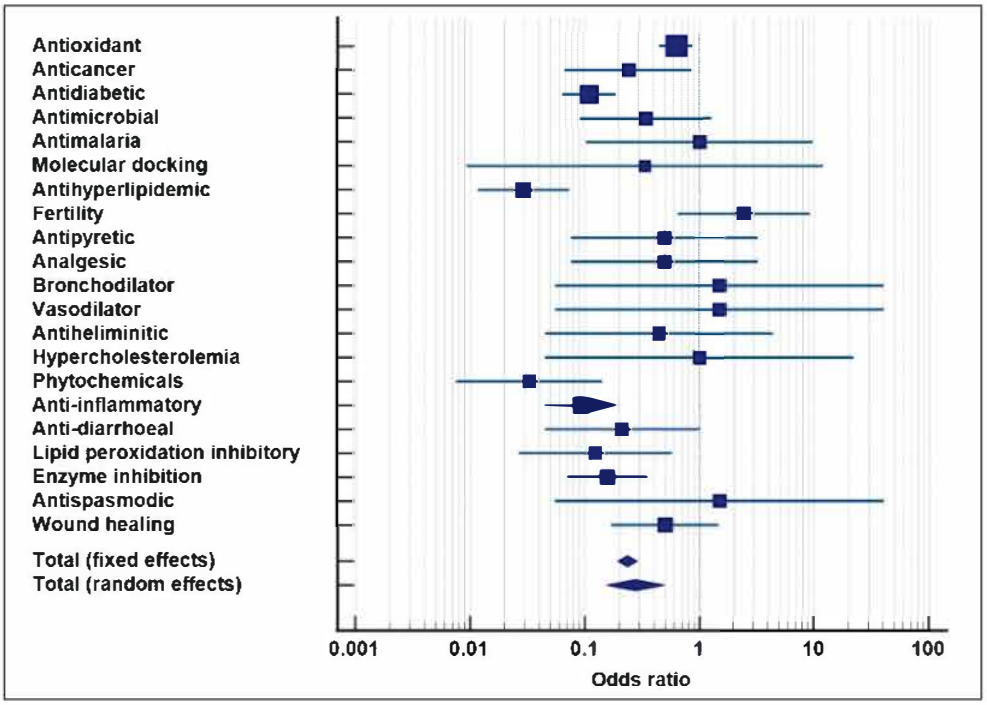

Fig. 6. Meta-analysis of Research methods in treating NCD with *Prosopis cineraria*

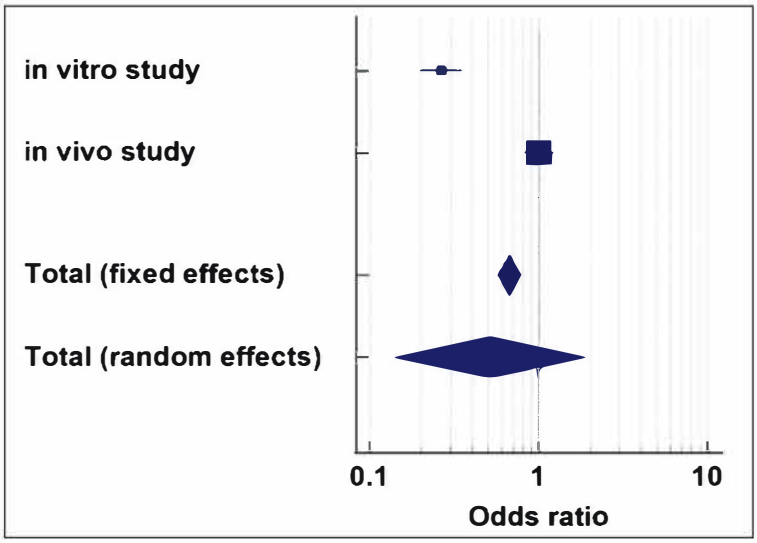

Fig. 7. Meta-analysis of the design of the study in treating NCD with *Prosopis cineraria*

Table 6 (a). Result of Meta-analysis of Research methods in treating NCD with *Prosopis cineraria*

Study	Intervention	Controls	Odds ratio	95% CI	z	P	Weight (%)	
							Fixed	Random
Antioxidant	568/785	236/293	0.632	0.455 to 0.878			40.70	7.58
Anticancer	75/98	40/43	0.245	0.0692 to 0.865			2.76	5.69
Antidiabetic	175/281	266/284	0.112	0.0654 to 0.191			15.39	7.29
Antimicrobial	57/90	15/18	0.345	0.0931 to 1.282			2.56	5.57
Antimalaria	3/6	3/6	1.000	0.104 to 9.614			0.86	3.57
Molecular docking	1/4	1/2	0.333	0.00931 to 11.939			0.34	1.97
Antihyperlipidemic	156/360	130/135	0.0294	0.0118 to 0.0736			5.23	6.51
Fertility	368/373	120/124	2.453	0.648 to 9.284			2.48	5.52
Antipyretic	6/18	3/6	0.500	0.0766 to 3.265			1.25	4.30
Analgesic	6/18	3/6	0.500	0.0766 to 3.265			1.25	4.30
Bronchodilator	3/5	1/2	1.500	0.0554 to 40.635			0.40	2.22
Vasodilator	3/5	1/2	1.500	0.0554 to 40.635			0.40	2.22
Anthelmintic	4/13	2/4	0.444	0.0452 to 4.374			0.84	3.53
Hypercholesterolemia	1/5	1/5	1.000	0.0451 to 22.176			0.46	2.43
Phytochemicals	72/228	28/30	0.0330	0.00764 to 0.142			2.06	5.21
Anti-inflammatory	76/144	120/130	0.0931	0.0452 to 0.192			8.41	6.93
Anti-diarrhoeal	10/30	7/10	0.214	0.0454 to 1.011			1.83	5.01
Lipid peroxidation inhibitory	4/36	6/12	0.125	0.0269 to 0.581			1.86	5.04
Enzyme inhibition	14/102	23/46	0.159	0.0709 to 0.357			6.75	6.76
Antispasmodic	3/5	1/2	1.500	0.0554 to 40.635			0.40	2.22
Wound healing	18/54	9/18	0.500	0.169 to 1.477			3.75	6.12
Total (fixed effects)	1623/2660	1016/1178	0.235	0.193 to 0.286	-14.416	<0.001	100.00	100.00
Total (random effects)	1623/2660	1016/1178	0.276	0.154 to 0.494	-4.334	<0.001	100.00	100.00

Table 6 (b). Test for heterogeneity and Publication bias of Research methods in treating NCD with *Prosopis cineraria*

Heterogeneity	
Q	98.4987
DF	20
Significancelevel	P < 0.0001
I^2 (inconsistency)	79.70%
95% CI for I^2	69.68 to 86.40

Publication bias	
Eggertest	
Intercept	-0.1703
95%CI	-1.8430 to 1.502
Significancelevel	P = 0.8335
Beggtest	
KendallTau	0.3107
Significancelevel	P= 0.0488

Table 7 (a). Result of Meta-analysis of Design of the study in treating NCD with *Prosopis cineraria*

Study	Intervention	Controls	Odds ratio	95% CI	z	P	Weight (%)	
							Fixed	Random
in vitro study	158/952	125/291	0.264	0.198 to 0.353			31.99	49.68
in vivo study	489/1604	199/654	1.003	0.823 to 1.222			68.01	50.32
Total (fixed effects)	647/2556	324/945	0.672	0.573 to 0.788	-4.889	<0.001	100.00	100.00
Total (random effects)	647/2556	324/945	0.517	0.140 to 1.912	-0.989	0.323	100.00	100.00

Table 7 (b). Test for heterogeneity and Publication bias of Design of the study in treating NCD with *Prosopis cineraria*

Heterogeneity	
Q	56.0604
DF	1
Significancelevel	P < 0.0001
I^2 (inconsistency)	98.22%
95% CI for I²	95.94 to 99.22

Publication bias	
Egger'stest	
Intercept	-28.8700
95%CI	
Significancelevel	P < 0.0001
Begg'stest	
Kendall'sTau	-1.0000
Significancelevel	P = 0.3173

types of research. Out of 22 research papers, 21 papers showed the therapeutic potential of *Prosopis cineraria* for treating NCDs. It has been shown that flavonoids and phenolic compounds present in *Prosopis cineraria* are active constituents and can reduce pulmonary inflammation (Dirar *et al.*, 2019). *In vitro* study shows that the ethanolic leaf and stem bark extracts of *Prosopis cineraria* show maximum antioxidant and antimicrobial activities due to the presence of phenolic and flavonoids as bioactive constituents. Though the molecular mechanism of *Prosopis cineraria* in improving conditions of NCDs remains primarily uninvestigated, fewer incidences of adverse effects are reported in research studies. The harmful adverse side effects of allopathic medicines compared to common side effects (dyspepsia, emesis, nausea, dermatitis) by administering herbal medicines satisfied the consumption level of herbal formulations globally (Posadzki *et al.*, 2013). Moreover, the positive effects of consuming *Prosopis cineraria* with other medications in combination need more investigation. The quality of research on herb-drug, and drug-drug interactions of *Prosopis cineraria* has to be emphasized in future studies. In this current systematic review, 22 studies from 18 publications were given priority as good impact studies showing positive outcomes.

Conclusion

Current evidence reveals that *Prosopis cineraria* as a folk medication indicated that mainly leaves and stem bark extracted by using ethanol, methanol, petroleum ether, butanol, ethyl acetate, and aqueous solvents were used as they contain bioactive constituents showing antidiabetic, anticancer, anti-inflammatory, antioxidant, antimicrobial, antihyperlipidemic potentials to treat NCDs also giving highly effective prediction ideas through computational biology. Further, *in vivo* and herb-drug interaction studies using wide-ranging randomized controlled trials (RCTs) are also required to confirm the therapeutic and pharmacological role of *Prosopis cineraria* in managing and treating NCDs.

References

Al-Saadoon, M., 2015. Adverse Effects of Medicines. Sultan Qaboos Univ. Med. J. 15, e149–e151.

Asati, V., Srivastava, A., Mukherjee, S., Sharma, P.K., 2021. Comparative analysis of antioxidant and antiproliferative activities of crude and purified flavonoid enriched fractions of pods/seeds of two desert legumes Prosopis cineraria and Cyamopsis tetragonoloba. Heliyon 7, e07304. https://doi.org/10.1016/j.heliyon.2021.e07304

Chaudhary, K.K., Kumar, G., Varshney, A., Meghvansi, M.K., Ali, S.F., Karthik, K., Dhama, K., Siddiqui, S., Kaul, R.K., 2018. Ethnopharmacological and Phytopharmaceutical Evaluation of Prosopis cineraria: An Overview and Future Prospects. Curr. Drug Metab. 19, 192–214. https://doi.org/10.2174/1389200218666171031125439

Choudhary, R.K., Saroha, A.E., Swarnkar, P.L., 2011. Radical scavenging activity of phenolics and flavonoids in some medicinal plants of India. J. Pharm. Res. 4(3):712-713.

Deshavath, N., Malothu, R., Reddy, R., Naadella, B., A.Elumalai, 2012. Evaluation of the *in-vivo* anti-diarrhoeal activity of *Prosopis cineraria* linn stem bark. Int. J. Biol. Pharm. Res. 3(3): 317-319.

Dirar, A.I., Alsaadi, D.H.M., Wada, M., Mohamed, M.A., Watanabe, T., Devkota, H.P., 2019. Effects of extraction solvents on total phenolic and flavonoid contents and biological activities of extracts from Sudanese medicinal plants. South Afr. J. Bot., Special Issue on Enzyme Inhibitors of natural origin. 120, 261–267. https://doi.org/10.1016/j.sajb.2018.07.003

Jain, P.G., Surana, S.J., 2015. Hypolipidemic Activity of Prosopis cineraria L (Druce) Fruit Extract and Molecular Modeling Study with Farnesoid X Receptor (FXR). Trop. J. Pharm. Res. 14, 1621–1628. https://doi.org/10.4314/tjpr.v14i9.11

Janbaz, K.H., Haider, S., Imran, I., Zia-Ul-Haq, M., De Martino, L., De Feo, V., 2012. Pharmacological Evaluation of Prosopis cineraria (L.) Druce in Gastrointestinal, Respiratory, and Vascular Disorders. Evid.-Based Complement. Altern. Med. ECAM 2012, 735653. https://doi.org/10.1155/2012/735653

Jangid, R., Jain, S., Sharma, M.K., Chatterjee, S., 2022. In vitro antioxidant and antidiabetic activity of ethanolic extract of Prosopis species growing in Rajasthan, India. Vegetos. https://doi.org/10.1007/s42535-022-00487-z

Jinu, U., Gomathi, M., Saiqa, I., Geetha, N., Benelli, G., Venkatachalam, P., 2017. Green engineered biomolecule-capped silver and copper nanohybrids using Prosopis cineraria leaf extract: Enhanced antibacterial activity against microbial pathogens of public health relevance and cytotoxicity on human breast cancer cells (MCF-7). Microb. Pathog. 105, 86–95. https://doi.org/10.1016/j.micpath.2017.02.019

Khatri, A., Rathore, A., Patil, U.K., 2011. Assessment of anthelmintic activity of the Prosopis cineraria (Linn.) Druce bark 2, 512–514.

Kumar, M., Govindasamy, J., Nyola, N.K., 2019. *In-vitro* and *in-vivo* Anti-Hyperglycemic Potential of *Prosopis cineraria* Pods Extract and Fractions. J. Biol. Act. Prod. Nat. 9, 135–140. https://doi.org/10.1080/22311866.2019.1588783

Liu, Y., Singh, D., Nair, M.G., 2012. Pods of Khejri (Prosopis cineraria) consumed as a vegetable showed functional food properties. J. Funct. Foods 4, 116–121. https://doi.org/10.1016/j.jff.2011.08.006

Manikandar, R.V.M., Rajesh, V., Kumar, R.S., Perumal, P., Raj, C.D., 2009. Analgesic and anti-pyretic activity of stem bark of Prosopis cineraria (Linn) Druce. J. Pharm. Res. 2, 660–662.

Mohammad, I.S., Muhammad, H., Khan, H.M. shoaib, Naveed, A., Rasool, F., 2013. Biological Potential and Phytochemical Evaluation of Prosopis cineraria. World Appl. Sci. J. 27, 1489–1494.

Nethan, S., Sinha, D., Mehrotra, R., 2017. Non Communicable Disease Risk Factors and their Trends in India. Asian Pac. J. Cancer Prev. APJCP 18, 2005–2010. https://doi.org/10.22034/APJCP.2017.18.7.2005

Nodushan, S.K.H., Emtiazy, M., Ardakani, M.E.Z., Salmani, M.H., Lotfi, M.H., 2020. Comparative Effect of *Prosopis cineraria* Ointment and Eucerin Softener on Eczema Area and Severity Index (EASI) score changes in Patients with Atopic Dermatitis. Arch Pharma Pract. 11(S1):61-66.

Pakkir Maideen, N.M., Velayutham, R., Manavalan, G., 2012. Protective Effect of Prosopis cineraria Against N-Nitrosodiethylamine Induced Liver Tumor by Modulating Membrane Bound Enzymes and Glycoproteins. Adv. Pharm. Bull. 2, 179–182. https://doi.org/10.5681/apb.2012.027

Posadzki, P., Watson, L.K., Ernst, E., 2013. Adverse effects of herbal medicines: an overview of systematic reviews. Clin. Med. Lond. Engl. 13, 7–12.

https://doi.org/10.7861/clinmedicine.13-1-7

Preeti, K., Sharma, R., Kumavat, R., 2017. Antimicrobial Activity of Different Parts of Prosopis cineraria. Adv. Biosci. Bioeng. 5, 78. https://doi.org/10.11648/j.abb.20170505.11

Ram, H., Jaipal, N., Charan, J., Kashyap, P., Kumar, S., Tripathi, R., Singh, B. P., Siddaiah, C. N., Hashem, A., Tabassum, B., Abd_Allah, E. F., 2020. Phytoconstituents of an ethanolic pod extract of Prosopis cineraria trigger the inhibition of HMG-CoA reductase and the regression of atherosclerotic plaque in hypercholesterolemic rabbits. Lipids Health Dis. (19)6: 1-11. https://doi.org/10.1186/s12944-020-1188-z

Ramalingam S, L., Vellapandian, C., R Vetrivelan, V., Sukumaran, E.S., 2020. Un-riped fruit pods of Prosopis cineraria (L.) Druce ameliorates Cisplatin therapy-induced partial testicular atrophy in male Wistar rats. J. Ethnopharmacol. 261, 113070. https://doi.org/10.1016/j.jep.2020.113070

Robertson, S., Narayanan, N., 2014. Isolation and characterization of secondary metabolite from Prosopis cineraria (L.) Druce for anticancer activity. World J Pharm Res. 3:876-884.

Robertson, S., Narayanan, N., Raj Kapoor, B., 2011. Antitumour activity of Prosopis cineraria (L.) Druce against Ehrlich ascites carcinoma-induced mice. Nat. Prod. Res. 25, 857–862. https://doi.org/10.1080/14786419.2010.536159

Satish, P.V.V., Somaiah, K., Brahmam, P., Rekha, N.S., Sunita, D.K., 2015. Antimalarial activity of *Prosopis cineraria* (L) Druce against Chloroquine sensitive *Plasmodium falciparum* 3D7 stain. European j. pharm. med. res. 2(7): 295-303.

Sharma, D., Singla, Y.P., 2015. Evaluation of the antihyperglycemic and antihyperlipidemic activity of *Prosopis cineraria* (Linn.) in Wistar rats. J. Sci. Innova. Res. 2(4): 751-758

Sharma, N., Garg, V., Paul, A., 2010. Antihyperglycemic, antihyperlipidemic and antioxidative potential of Prosopis cineraria bark. Indian J. Clin. Biochem. IJCB 25, 193–200. https://doi.org/10.1007/s12291-010-0035-9

Sharma, V., Sharma, P., Sharma, K., 2020. Unfolding the antioxidative and free radicals scavenging potential of stem bark of the wonder tree, Prosopis cineraria (L.) Druce: An in vitro approach. Int. J. Green Pharm. IJGP 14. https://doi.org/10.22377/ijgp.v14i1.2865

Sharma, V., Sharma, P., 2020. Phyto-therapeutic potential of stem bark of the wonder tree, Prosopis cineraria (L.) Druce in LPS-induced mouse model: An Anti-Inflammatory Study. Clin. Phytoscience 6, 45. https://doi.org/10.1186/s40816-020-00168-x

Soni, L.K., Basak, A., Parasher, P., Dobhal, M.P., 2015. Free radical scavenging activity of Urginea indica, Alhagi maurorum, Crinum asiaticum and Prosopis cineraria. Int. J. Pharm. Phytochem. Res. 7:311-314.

Soni, L.K., Dobhal, M.P., Arya, D., Bhagour, K., Parasher, P., Gupta, R.S., 2018. In vitro and in vivo antidiabetic activity of isolated fraction of Prosopis cineraria against streptozotocin-induced experimental diabetes: A mechanistic study. Biomed. Pharmacother. Biomedecine Pharmacother. 108, 1015–1021. https://doi.org/10.1016/j.biopha.2018.09.099

Sundaravadivelu, S., 2012. Influence of curcuma amada and Prosopis cineraria leaf extracts in human breast cancer cell line. J Cancer Sci Ther. 4(10):136.

Velmurugan V., Arunachalam G., Ravich V., ran., 2011. The anthelmintic potential of *Prosopis cineraria* (Linn.) Druce stems barks. Asian J. Plant Sci. Res. 1(2):88-91.

Wachtel-Galor, S., Benzie, I.F.F., 2011. Herbal Medicine, Herbal Medicine: Biomolecular and Clinical Aspects. 2nd edition. CRC Press/Taylor & Francis.

Wang, Y., Wang, J., 2020. Modelling and prediction of global non-communicable diseases. BMC Public Health 20, 822. https://doi.org/10.1186/s12889-020-08890-4

World Health Organization, 2011. Global status report on noncommunicable diseases 2010.

Yadav, E., Singh, D., Yadav, P., Verma, A., 2018. Antioxidant and anti-inflammatory properties of Prosopis cineraria based phenolic rich ointment in wound healing. Biomed. Pharmacother. Biomedecine Pharmacother. 108, 1572–1583. https://doi.org/10.1016/j.biopha.2018.09.180