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RESEARCH ARTICLE

PASS Assisted Prediction and Meta-analysis of Active Phytoconstituents of *Guggul* for the Treatment of Chronic Prostatitis: A Gateway to Cure Prostate Cancer

Vinayak Bhushan and Rakesh K. Sindhu*

School of Pharmacy, Sharda University, Greater Noida, Gautam Buddha Nagar – 201310, Uttar Pradesh, India; drrakeshksindhu@gmail.com

Abstract

Background: Mostly men are particularly prone to prostate cancer as well as chronic prostatitis the underlying causes behind prostate cancer as well as chronic prostatitis are multifaceted as well as diverse a spike in serum prostate-specific antigen characterises both diseases. Chronic prostatitis is prostate inflammation independent of the source inflammation and is linked to a variety of malignancies in general along with prostate inflammatory reactions that are thought to have a contributing influence on the advancement and growth of prostate cancer. **Aim:** This study aims to identify different phytoconstituents of *Guggulu* for treating chronic prostatitis along with meta-analysis. Meta-analysis is used as an analytical technique to aggregate results of separate inferential statistics investigations of clinical data on chronic prostatitis. **Methods:** Phytochemical ingredients were analyzed using PASS estimates. Canonical SMILES were identified to determine Pa values. PASS software was then used to forecast activities. Doxycycline, a conventional drug for chronic prostatitis, was selected for comparison. Data was collected using the PASS online program to estimate physiological and biochemical parameters. The activities of all constituents were then compared against doxycycline. **Results:** The results indicate that *Guggul* sterone Z shows promise as a candidate for further investigation in medication therapy for chronic prostatitis. A meta-analysis aims to identify clinical trials for this phytoconstituent, which has yielded the highest number of results. PASS prediction findings reveal that *Guggul* sterone Z, followed by Mansumbinone, 16-dehydroprogesterone, and alpha-pinene, exhibit the most significant activities. **Conclusion:** The study forecasted that *Guggul* sterone Z, Mansumbinone, 16-dehydroprogesterone and alpha-pinene are the potential phytoconstituents that can play a vital role in the development of novel treatments for chronic prostatitis-induced prostate cancer.

Keywords: Inflammation, *Guggul*, Meta-analysis, PASS, Prostate Cancer, Prostatitis

1. Introduction

Chronic inflammatory diseases have been associated with the formation of tumours in the liver, colon, bladder, oesophagus, and stomach. By being exposed to potent chemicals and growth hormones[1]. The existing classification scheme for prostatitis consists of four categories: acute bacterial, chronic bacterial, chronic non-bacterial (inflammatory), and chronic pelvic pain syndrome. Prostatitis may contribute to the development of prostate cancer and be carcinogenic[2] (Figure 1).

Proliferative inflammatory atrophy has been hypothesized to represent an initial stage lesion of prostate cancer, characterized by pathological alterations. Chronic inflammatory processes may contribute to the development of other types of cancer, such as prostate cancer. One crucial piece of evidence supporting this hypothesis is derived from epidemiological studies of clinical prostatitis, which is

*Author for correspondence

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essentially inflammation of the prostate gland. Meta-analyses of these investigations have revealed significant positive correlations between clinical prostatitis and prostate cancer, indicating that prostate inflammation may play a pivotal role in the development of prostate cancer. *Guggulu* is composed of a diverse mixture of steroids, amino acids, aliphatic esters, diterpenes, lignans, and many inorganic compounds, as stated in prior research.

The persistent inflammatory microenvironment can facilitate the development of both inflammation in the prostate and cancer. These two conditions are connected through both intrinsic and extrinsic molecular and cellular mechanisms. In the intrinsic mechanism, oncogenes are both activated and induced to express programs related to inflammation. Extrinsic inflammation promotes the advancement of cancer in situations when a pro-inflammatory environment is present.

The main objective of this study was to assess the robustness and reliability of the observed connections between prostatitis and prostate cancer by analyzing various phytoconstituents of *Guggulu*. Furthermore, a comprehensive meta-analysis was conducted to determine the clinical importance of different phytoconstituents of *Guggulu* in treating prostatitis.

Guggulu, also known as *Commiphora wightii*, has long been used in Indian traditional medicine to treat rheumatoid arthritis, inflammation, obesity, and hyperlipidemia. Other investigations on *Guggulu* have shown that it has a wide range of medical properties, including anti-microbial, anti-inflammatory, and anti-cancer properties[3]. According to earlier research, *Guggulu* includes a complex mixture of steroids, amino acids, aliphatic esters, diterpenes, lignans, and other inorganic compounds[5]. The oleogum resin, also known as *Guggulu* lipid, is a yellow viscous liquid that includes several active medicinal components with a variety of actions, including α-camphorene and *Guggul* sterone. Despite breakthroughs in surgery, radiation, medical treatment, and surveillance, prostate cancer remains a leading cause of morbidity.

The olefins of the *Guggulu* plant are indeed a unique combination comprising gum, elements, essential oils, terpenes, sterols, ferrulates, flavanones and sterones. Plenty more unidentified chemicals were also discovered. Following ethyl acetate treatment, the resin yields two portions of extract. "The ethyl acetate-soluble portion contains 45% of the gum resin. The intractable percentage is made up of carbohydrate gum which accounts for around 55% of the gum resin. These bioactive molecules were identified in the ethyl acetate-soluble fraction, while the refractory carbohydrate". There have been no hypolipidemic repercussions by this portion.

The *Guggulu* tree classified as part of the Burseraceae family is predominant in the dry parts of the Indian peninsula specifically in countries such as India, Pakistan as well as Bangladesh. *Guggulu* tree (*Commiphora mukul*) oleogum resin is a yellowish matter gathered throughout the colder months and every specimen generates 700–900 g of resin[6].

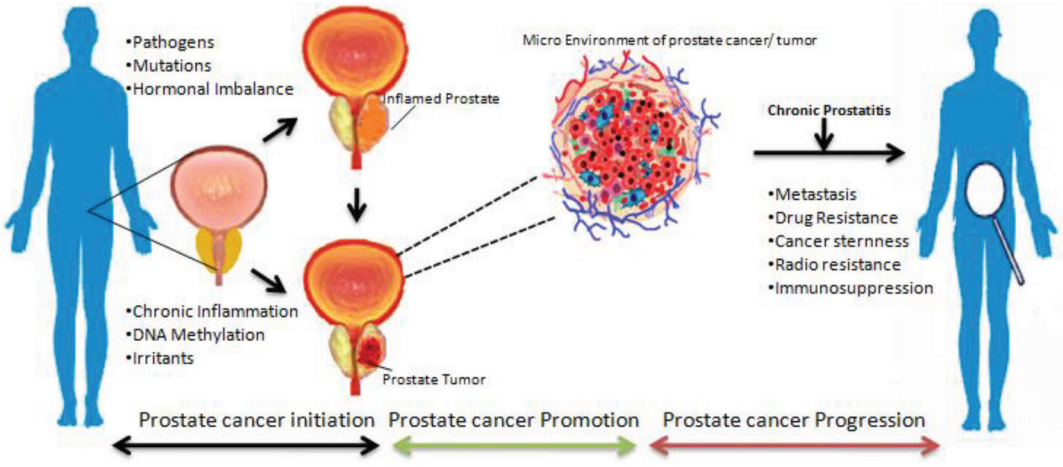


Figure 1. A graphical representation of the relationship between chronic inflammation and various phases of prostate carcinogenesis, such as prostate cancer start, promotion, and advancement.

Table 1. Phytochemicals are canonical. SMILES along with their chemical structures

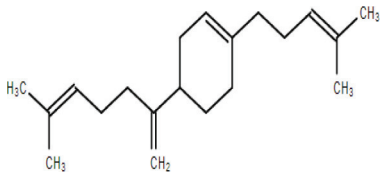
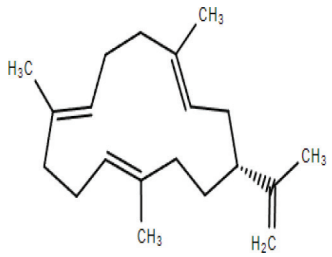
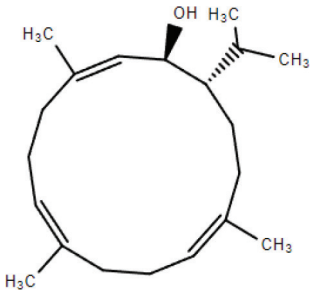
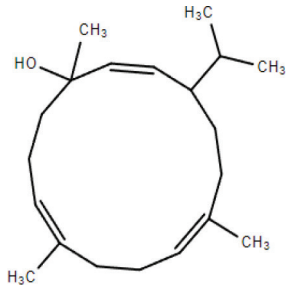
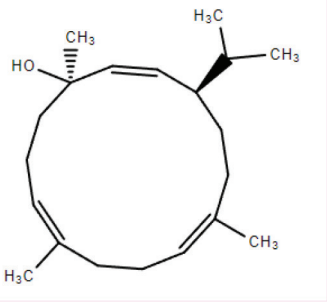
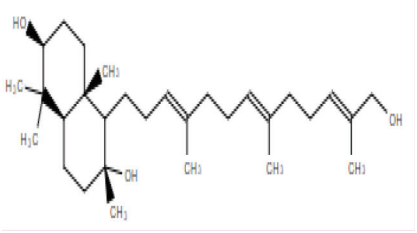
Phytoconstituents Name	Canonical SMILES	Molecular Weight	Chemical structure
α-Camphorene	CC(=CCCC1=CCC(C C1)C(=C)CCC=C ©C)C	272.5 g/mol	
Cembrene-A	CC1=CCCC(=CC C(CCC(=CCC1)C) C(=C)C)C	272.5 g/mol	
Mukulol	C/C/1=C/CC/C(=C \[C@@H]([C@@ H] (CC/C(=C\CC1) /C)C©C)O)/C	290.5 g/mol	
Isocembrol	C/C/1=C/CCC(/C=C\C(CC/C(=C\CC1)/C) C©C)©O	290.5g/mol	
4-Epiisocembrol	C/C/1=C\CC[C@@](/C=C/[C@H](CC/C(=C\ CC1)/C)C©C)©O	290.5g/mol	
Myrrhanol A	C/C/1=C\CC[C@@](/C=C/[C@H](CC/C(=C\ CC1)/C)C©C)©O	290.5g/mol	

Table 1. Continued...

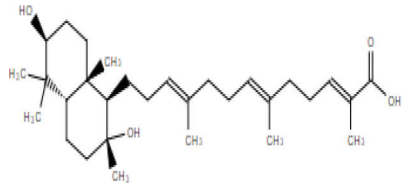
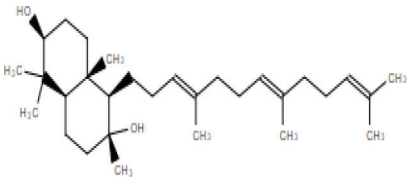
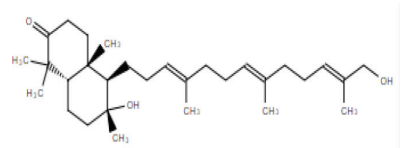
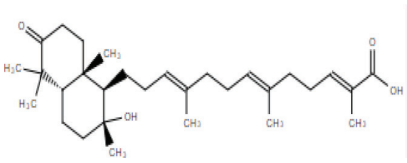
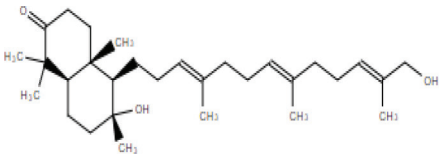
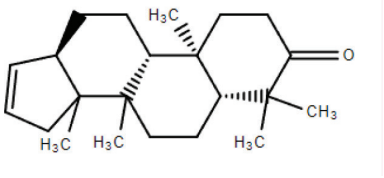
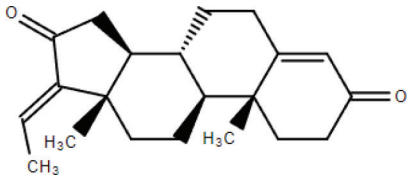
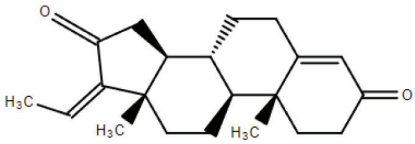
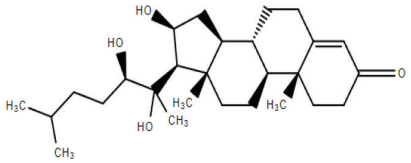
Phytoconstituents Name	Canonical SMILES	Molecular Weight	Chemical structure
Myrrhanol B	C/C(=C\CC[C@@H]1[C@]2(CC[C@@H](C([C@H]2CC[C@@]1©O)©C)O)C)/CC/C=C(\C)/CC/C=C(\C)/C(=O)O	474.7g/mol	
Myrrhanol C	CC(=CCC/C(=C/CC/C(=C/CC[C@@H]1[C@]2(CC[C@@H](C([C@@H]2CC[C@@]1©O)©C)O)C)/C)/C)C	444.7g/mol	
Myrrhanone A	C/C(=C\CC[C@@ H]1[C@]2(CCC(=O)C([C@H]2CC[C@@]1©O)©C)C)/ CC/C=C(\C)/CC/C=C(\C)/CO	458.7g/mol	
Myrrhanone B	C/C(=C\CC[C@@ H]1[C@]2(CCC(=O)C([C@H]2CC[C@@]1©O)©C)C)/ CC/C=C(\C)/CC/C=C(\C)/C(=O)O	472.7g/mol	
Commipherol	C/C(=C\CC[C@@ H]1[C@]2(CCC(=O)C([C@@H]2CC[C@@]1©O)©C) C)/CC/C=C(\C)/C C/C=C(\C)/CO	458.7g/mol	
Mansumbinone	C[C@]12CCC(=O)C([C@@H]1CC[C@@]3([C@@H]2CC[C@H]4[C@]3(CC=C4)C)C)©C	314.5g/mol	
E- Guggul sterone	C/C=C\1/C(=O)C[C@@H]2[C@@]1(CC[C@H]3[C@H]2CCC4=CC(=O)CC[C@]34C)C	312.4g/mol	
Z-Guggul sterone	C/C=C/1\C(=O)C[C@@H]2[C@@]1(CC[C@H]3[C@H]2CCC4=CC(=O)CC[C@]34C)C	312.4g/mol	
Guggul sterol-I	CC©CC[C@H](C©([C@H]1[C@H](C[C@@H]2[C@@]1(CC[C@H]3[C@H]2CCC4=CC (=O)CC[C@]34C) C)O)O)O	432.6g/mol	

Table 1. Continued...

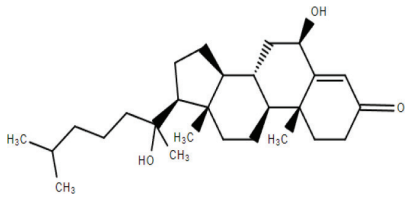
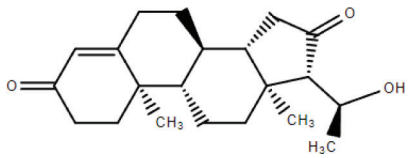
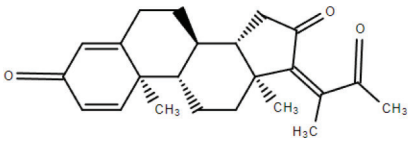
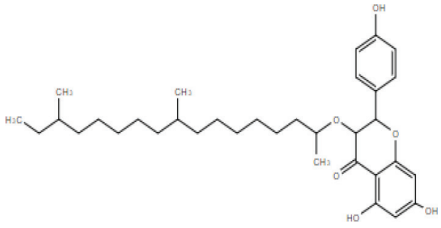
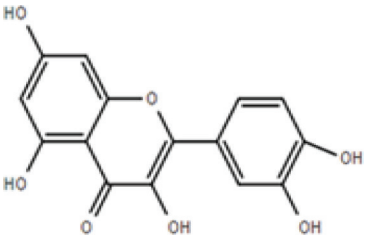
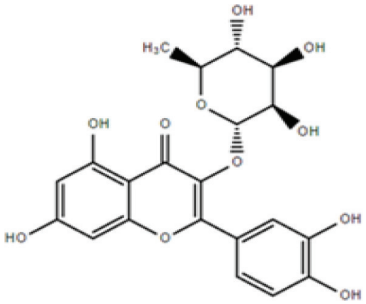
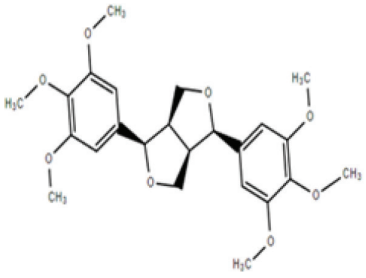
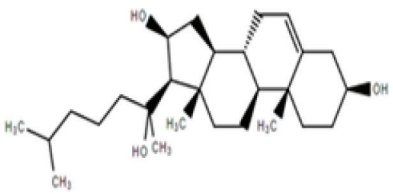
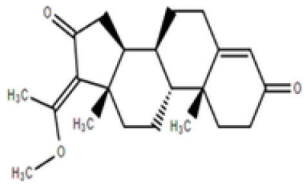
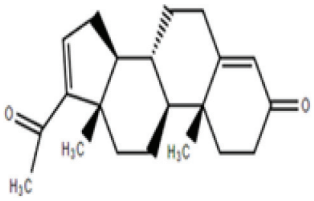
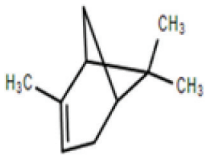
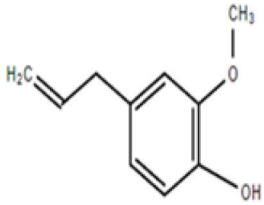
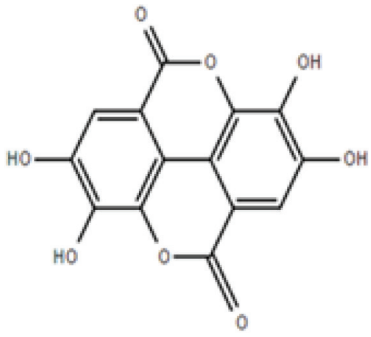
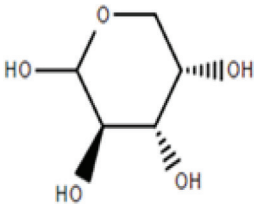
Phytoconstituents Name	Canonical SMILES	Molecular Weight	Chemical structure
Guggul sterol-III	CC©CCCC©([C@ H]1CC[C@@H]2[C@@]1(CC[C@H]3[C@H]2C[C@H] (C4=CC(=O)CC[C@]34C)O)C)O	416.6g/mol	
4-Pregnene-3,16-dione	C[C@@H]([C@H]1C(=O) C[C@@H]2[C@@]1(CC[C @H]3[C@H]2CC C4=CC(=O)CC[C @]34C)C)O	330.5g/mol	
Dehydro Guggulsterone-M	C/C(=C\1/C(=O)C[C@@H]2[C@@]1	352.5g/mol	
Muscanone	(CC[C@H]3[C@H]2CCC4=CC(=O) C=C[C@]34C)C)/C(=O)C	554.8g/mol	
Quercetin	CCC©CCCCCC© CCCCCCC©OC1 C(OC2=CC(=CC(=C2C1=O)O)O) C3=CC=C(C=C3)O	302.2g/mol	
Quercetin-3-O-α-L-rhamnoside	C1=CC(=C(C=C1 C2=C(C(=O)C3=C (C=C(C=C3O2)O) O)O)O)O	448.4g/mol	
Diayangambin	C[C@H]1[C@@H]([C@H]([C@H]([C@@H] (O1)OC2=C(OC3=CC(=CC (=C3C2=O)O)O) C 4=CC(=C(C=C4)O)O)O)O)O	446.5g/mol	

Table 1. Continued...

Phytoconstituents Name	Canonical SMILES	Molecular Weight	Chemical structure
Guggulsterol-II	COC1=CC(=CC(= C1OC)OC)[C@H] 2[C@H]3CO[C@ H]([C@H]3CO2)C 4=CC(=C(C(=C4) OC)OC)OC	418.7g/mol	
Guggul sterone-M	CC(C)CCCC(C)([C@H]1[C@H] (C[C@@H]2[C@@]1 (CC[C@H]3[C@H]2CC=C4[C@@]3 (CC[C@@H](C4)O)C)C)O)O	342.5g/mol	
16-dehydro progesterone	C/C(=C/1\C(=O)C[C@@H]2[C@@]1 (CC[C@@H]3[C @@H]2CCC4=CC (=O) CC[C@]34C) C)/OC	312.4g/mol	
Alpha-Pinene	CC(=O)C1=CC[C@@H]2[C@@]1(CC[C@H]3[C@H]2CCC4=CC(=O)C C[C@]34C)C	136.23g/ mo l	
Eugenol	CC1=CCC2CC1C 2(C)C	164.2g/mol	
Ellagic acid	C1=C2C3=C(C(=C 1O)O)OC(=O)C4= CC(=C(C(=C43)O C2=O)O)O	302.2g/mol	
L-arabinose	C1[C@@H]([C@ @H]([C@H](C(O1)O)O)O)O	150.1g/mol	

Commiphora mukul has previously been extensively studied for cancer treatment *Guggul* sterone as well as *Guggul*lipid (GL) were used to treat a variety of ailments they have also been discovered to influence several elements of cancer they also prevent metastasis angiogenesis along with cell proliferation in PC-3 cells. *Guggul* sterone fosters apoptosis in an amount-dependent manner[7,31-34].

The following natural substances have therapeutic and preventive actions in chronic prostatitis:

2. Materials and Methods

The PASS approach relies on analyzing the Structure-Activity Relationships (SARs) of the training dataset, which presently comprises around 46,000 pharmaceuticals, active chemicals, and major compounds that have been experimentally demonstrated to have biological activity. The SARs are acquired throughout the training phase and stored in the SAR Base, a repository of information. PASS chemical descriptors utilize the multi-level communities of atoms that were previously defined[1,9].

To investigate the pharmacological properties of selected phytoconstituents against chronic prostatitis. First, we must select the canonical Simple Molecular-Input Line-Entry System (SMILES) from the PubChem website as shown in Figure 2. That pasted in the PASS software by clicking on the "predict activity" several activities are shown by software with Pa and Pi values. We used the Pa value for evaluating the activities of the phytoconstituents. These SMILES serve as the molecule's molecular formula and are quickly entered into the PASS algorithm to assess activity[10].

3. Meta-analysis

Gene indicates meta-analysis as a scientific finding out of a diverse number of numerical analyses it is a quanway to calculate anticipated intended output by incorporating overall findings from multiple investigations and assessing information from various independent studies for the same sample[11].

Meta-analysis is used as an analytical technique to aggregate results of separate inferential statistics investigations there are two types of meta-analysis work evaluations of the statistically significant aggregated outcome approaches for merging estimations across investigations the distinct kinds of combined significance analysis are covered also their constraints fixed effect regression techniques deal with the effect magnitude parameters that must be calculated as

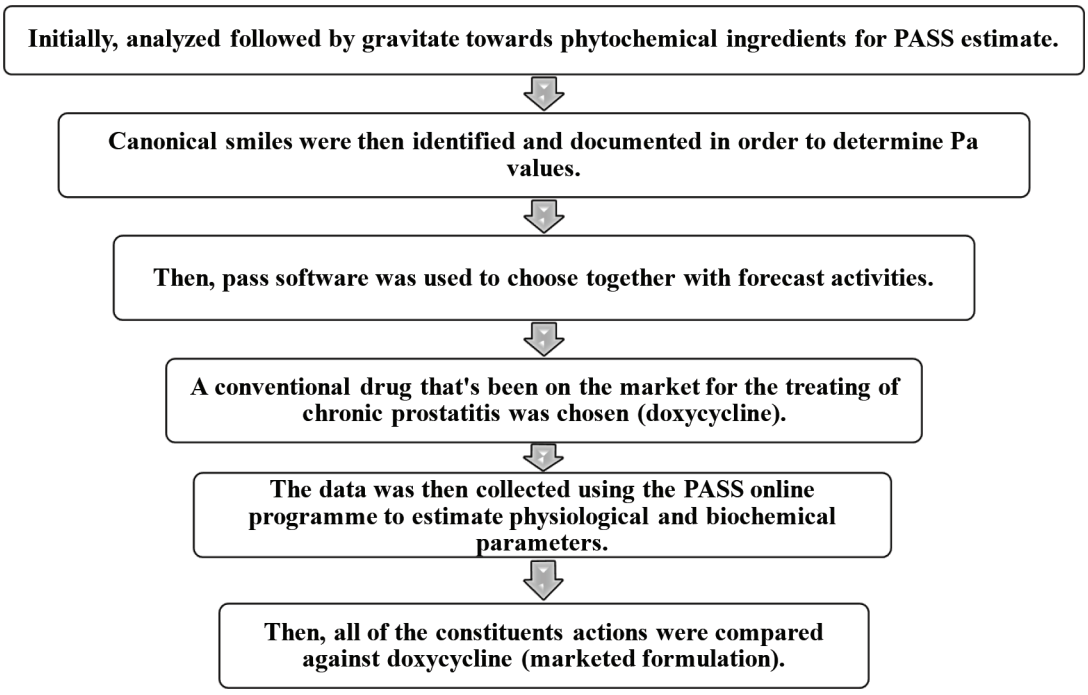


Figure 2. Flow chart for depicting the process of PASS prediction.

a result of a model that includes constant though uncertain variables[12,13].

3.1 For conducting Meta-analysis

The CAMARADES, as well as PRISMA criteria, are implemented while doing a meta-analysis for such indicated phytoconstituent of clinical information. All clinical studies incorporating the specified phytoconstituents are therefore gathered to do the meta-analysis. Furthermore, depending on the clinical information that has been retrieved, comparable parameters are chosen for all clinical investigations that are focused here on symptoms of chronic prostatitis.

This study also includes exclusion and inclusion parameters gathered through clinical studies. To optimize the acquisition of all feasible evidence, "the exclusion and inclusion criteria" for designated phytoconstituents underlying chronic prostatitis in humans were defined[18].

3.2 Selection for Clinical Criteria

Data inclusion and exclusion were carried out to obtain clinical criteria. Clinical data were evaluated if the studies included in the data below were accessible: -

The following are the inclusion criteria:

- Randomized, open clinical, double-blinded clinical trial expressed by the study.
- The participation of humans was included.
- Selected phytoconstituent should be administered.
- Modified Boyarsky scoring system, international prostate symptoms score and AUA symptom.
- Patients of either sex, age 18-65 years.
- The following are the exclusion criteria:
- Patients aged less than 18.
- Sample sizes, standard deviation and means were not mentioned in the study.
- Administration of specified phytoconstituents is not present.
- The study's data was not available in English.
- Articles with insufficient abstracts and titles.

4. Collection of Data

The following guidelines were used to choose data from clinical studies. PRISMA and CAMARADES recommendations. Study characteristics, and subject information such as (health condition, age, gender), and intervention type (e.g.: phytoconstituent, composition, and duration). Outcome of data (mean value of effect, group sample sizes, variation in groups). "The outcome of data was included if it was generated through an assessment of chronic prostatitis symptoms over similarity was acceptable for all meta-analyses. The Cochrane Collaboration's risk of bias measure was utilized for clinical research". In addition, Review Manager 5 software was employed for the research in which the standard values were lacking.

5. Search Strategy

The evaluated literature was gathered utilizing database tools such as PubMed, Google Scholar, PMC and Science Direct from the beginning of time until August 2023 the major words employed for locating relevant paper references are phytoconstituents chronic prostatitis human research and humans the scientific papers that are related to the research investigations are also provided as references in this study the abstract and title of the discovered relevant studies met the inclusion criteria for effective data assessment and entire textual articles were estimated to evaluate study inclusion for the meta-analysis quantification and assessment were done consistently for clinical evaluation as shown in Figure 3.

6. Methodology of Calculating the Odds Ratio

In our investigation, we initially searched the literature from several databases to analyze the article or study of interest in the public domain to acquire clinical data for the meta-analysis. For the computation of Odds Ratios (ORs), we used the following methods:

- We determined the positive (bad) and negative (good) findings of our interest by reading each literary text.
- We chose the improvement of the NIH-Chronic Prostatitis Symptom Index (CPSI) for the clinical studies in the case of ellagic acid, prostate weight reduction in Z-*Guggul* sterone, (NIH SYMPTOM SCORE) and International Prostate Symptom Score (IPSS) in Quercetin as our negative (good) outcome of interest.

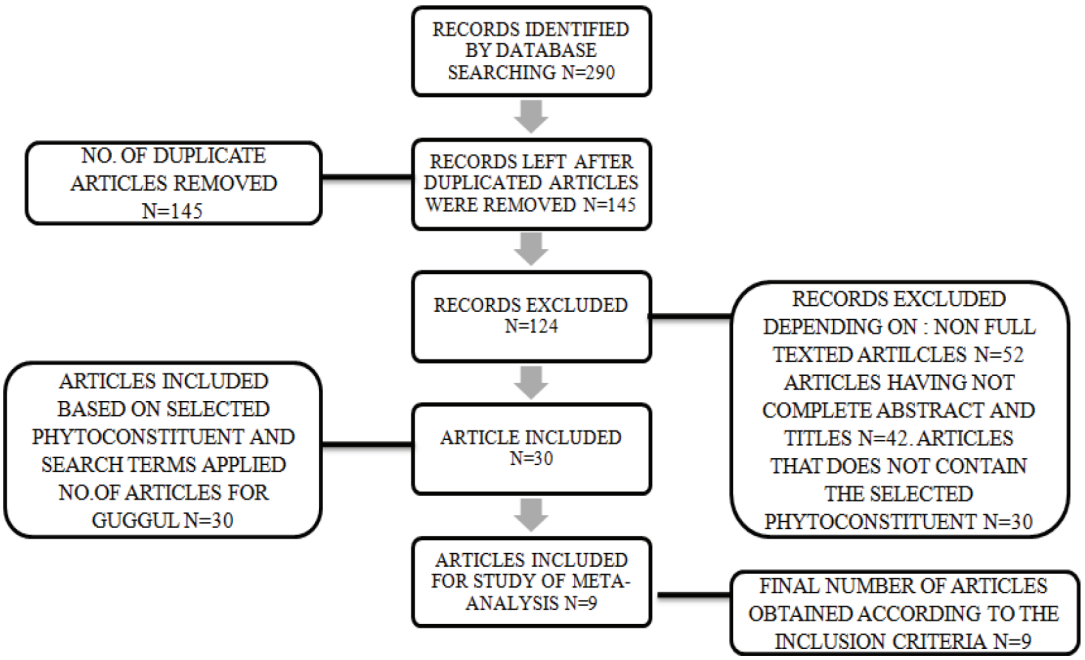


Figure 3. Flow chart for selection of clinical studies.

- We considered the less improved data of NIH-Chronic Prostatitis Symptom Index (CPSI) in the case of ellagic acid, prostate weight reduction in Z-*Guggul* sterone, (NIH SYMPTOM SCORE) and International Prostate Symptom Score (IPSS) in Quercetin for the clinical studies as our positive (bad) outcome of interest.
- The ORs for the meta-analysis were calculated using the free online software MEDCALC (https://www.medcalc.org/calc/odds ratio.php). We chose the improvement of the NIH-Chronic Prostatitis Symptom Index for the clinical studies (CPSI).
- We plotted the values after calculating the ORs and 95 per cent Confidence Intervals (CIs) in Microsoft Excel.
- Last, the forest plots for the factors NIH-Chronic Prostatitis Symptom Index (CPSI) in case of ellagic acid, prostate weight reduction in Z-*Guggul* sterone, (NIH SYMPTOM SCORE) and International Prostate Symptom Score (IPSS) in Quercetin using the "Odds ratio for the clinical study is then plotted".

7. Results

In Table 1 the Phytochemicals having canonical SMILES along with their chemical structures from PubChem software demonstrate how a specific phytochemical and commercial molecule were predicted using PASS for ten actions in chronic prostatitis. Among these activities are the following:

Apoptosis Agonist
Caspase 3 stimulant
Prostate disorders treatment
Transcription factor NF kappa B inhibitor
Testosterone 17beta-dehydrogenase (NADP+) inhibitor
Interleukin 6 antagonist
TNF expression inhibitor
Caspase 8 stimulant
Interleukin 1a antagonist
Anti-inflammatory

Guggulu has been shown to cause "apoptosis in cancer cells by repression of NF-B, activation of JNK, and reduced expression of Akt and anti-apoptotic proteins in vitro studies"[14,19] implying that it could trigger the same apoptosis in a patient with chronic prostatitis-induced prostate cancer[20-28]. In this study, we chose phytochemical components that are effective in both "*in vitro*" and "*in vivo*" investigations of chronic prostatitis models. All compounds were tested for the major ten activities shown in Table 2. *Guggul* sterone Z has the highest value for chronic prostatitis therapy, whereas Cambrene-A has the lowest. It demonstrates that *Guggul* sterone Z may ameliorate chronic

Table 2. PASS activity of selected phytoconstituents

Name of compounds	Apoptosis Agonist	Caspase 3 stimulant	Prostate disorders treatment	Transcription factor NF kappa B inhibitor	Testosterone 17 beta-dehydrogenase (NADPH+) inhibitor	Interleukin 6 antagonist	TNF expression inhibitor	Caspase 8 stimulant	Interleukin 1a antagonist	Anti-inflammatory
α-Camphorene	0.872	0.558	0.355	NP	0.558	NP	NP	0.295	NP	0.749
Cembrene-A	0.391	0.321	0.401	NP	NP	NP	0.478	0.263	NP	0.656
Cembrene	0.391	0.321	0.401	NP	0.73	0.191	0.478	0.263	NP	0.656
Mukulol	0.506	0.432	0.298	NP	0.832	0.227	0.485	0.326	0.094	0.708
Isocembrol	0.391	0.28	0.404	0.265	0.637	0.182	0.412	0.297	NP	0.48
4-Epiisocembrol	0.391	0.28	0.404	0.265	0.637	0.182	0.412	0.297	NP	0.48
Myrrhanol A	0.672	0.28	0.357	0.385	0.677	0.214	0.575	0.525	NP	0.616
Myrrhanol B	0.691	0.732	0.352	0.55	0.738	0.32	0.532	0.526	NP	0.604
Myrrhanol C	0.742	0.701	0.412	0.565	0.78	0.239	0.59	0.54	NP	0.633
Myrrhanone A	0.699	0.318	0.399	0.257	0.649	NP	0.629	0.367	NP	0.632
Myrrhanone B	0.725	0.399	0.395	0.424	0.701	0.18	0.579	0.367	NP	0.621
Commipherol	0.699	0.318	0.399	0.257	0.649	NP	0.629	0.367	NP	0.632
Mansumbinone	0.864	0.757	0.684	0.25	0.898	0.19	0.395	0.615	0.084	0.642
E- *Guggul* sterone	0.525	0.423	0.755	0.218	0.972	0.533	NP	0.534	0.12	0.564
Z- *Guggul* sterone	0.525	0.423	0.755	0.758	0.972	0.197	0.533	0.534	0.92	0.564
*Guggul*sterol-I	0.53	0.537	0.665	0.164	0.972	NP	0.61	0.33	0.09	0.559
*Guggul*sterol-II	0.803	0.813	0.69	0.343	0.944	NP	0.336	0.44	0.083	0.0599
*Guggul*sterol-III	0.613	0.637	0.662	0.402	0.965	NP	0.484	0.372	0.083	0.599
4-Pregnene-3,16-dione	0.402	0.296	0.723	0.11	0.972	NP	0.651	0.389	0.105	0.514
Dehydro *Guggul* sterone-M	0.537	0.555	0.723	0.256	0.927	NP	0.528	0.486	0.1	0.853
Muscanone	0.594	0.46	NP	0.116	0.464	0.178	0.583	0.283	NP	0.702
Quercetin	0.887	0.499	NP	0.334	0.714	0.26	0.501	0.428	NP	0.689
Quercetin-3-O-α-L-rhamnoside	0.814	0.803	NP	0.387	0.364	0.538	0.226	0.636	NP	0.754
Diayangambin	0.495	0.766	0.378	0.394	0.715	NP	0.435	0.49	0.083	0.489
Guggul sterone-M	0.891	0.635	0.758	0.293	0.377	0.221	0.593	0.599	0.127	0.561
16-dehydro progesterone	0.492	0.383	0.781	0.288	0.972	0.197	0.63	0.455	0.103	0.636
alpha-Pinene	0.377	0.397	0.371	0.257	0.863	0.236	0.348	0.438	0.113	0.49
Eugenol	0.743	0.873	NP	0.488	0.644	0.207	0.525	0.598	0.107	0.491
Ellagic acid	0.709	0.491	NP	0.276	0.85	0.256	0.412	0.47	0.087	0.749
L-arabinose	0.63	0.491	NP	0.195	0.813	0.291	0.249	0.773	0.106	0.777
Doxycycline	NP	NP	0.978	0.398	0.759	NP	0.262	NP	NP	NP

prostatitis-induced prostate cancer by acting on several mechanisms.

For meta-analysis - the phytoconstituents selected demonstrated a significant number of results when subjected to clinical studies. The greatest number of studies were discovered for the phytoconstituents Z-*Guggul* sterone, quercetin, and ellagic Acid, which also covered a wide range of active targets in the Pass prediction results as shown in Figure 4. As a result, the emphasis of this meta-analysis is on the identification of clinical trials including the chosen phytoconstituent for chronic prostatitis.

7.1 Clinical Studies Characteristic

The Clinical studies characteristic of different phytoconstituents are shown in Table 3.

In cases where no standard mean was provided, the SD was calculated using RevMan5 software using the supplied confidence interval values. In cases where no standard mean was provided, The SD was calculated using RevMan5 software using the supplied confidence interval values. According to[14], "an OR of 1 indicates that there is no difference between the approximated and observed estimates, an OR greater than 1 indicates that the approximated value overestimates, and an OR < 1 indicates that the approximated value underestimates the observed treatment effect. The observed and estimated odds ratios were derived from the same data set and were associated. Also, when the OR=1 value is reached, it shows that the computed value has a considerable influence, i.e. it is beneficial, however when the OR value is smaller or looks to be negative, it suggests that there is no significant impact on the disease".

"So, given below are the figures that depict the forest plot of the clinical studies".

The Figure 5 the Ors (95% CI) of studies 1 and 2 for NIH-Chronic Prostatitis Symptom Index (CPSI) with phytoconstituent (ellagic acid) treatment are 1.4933 (0.5815 to 3.8349) and 2.3333 (1.0026 to 5.4301)

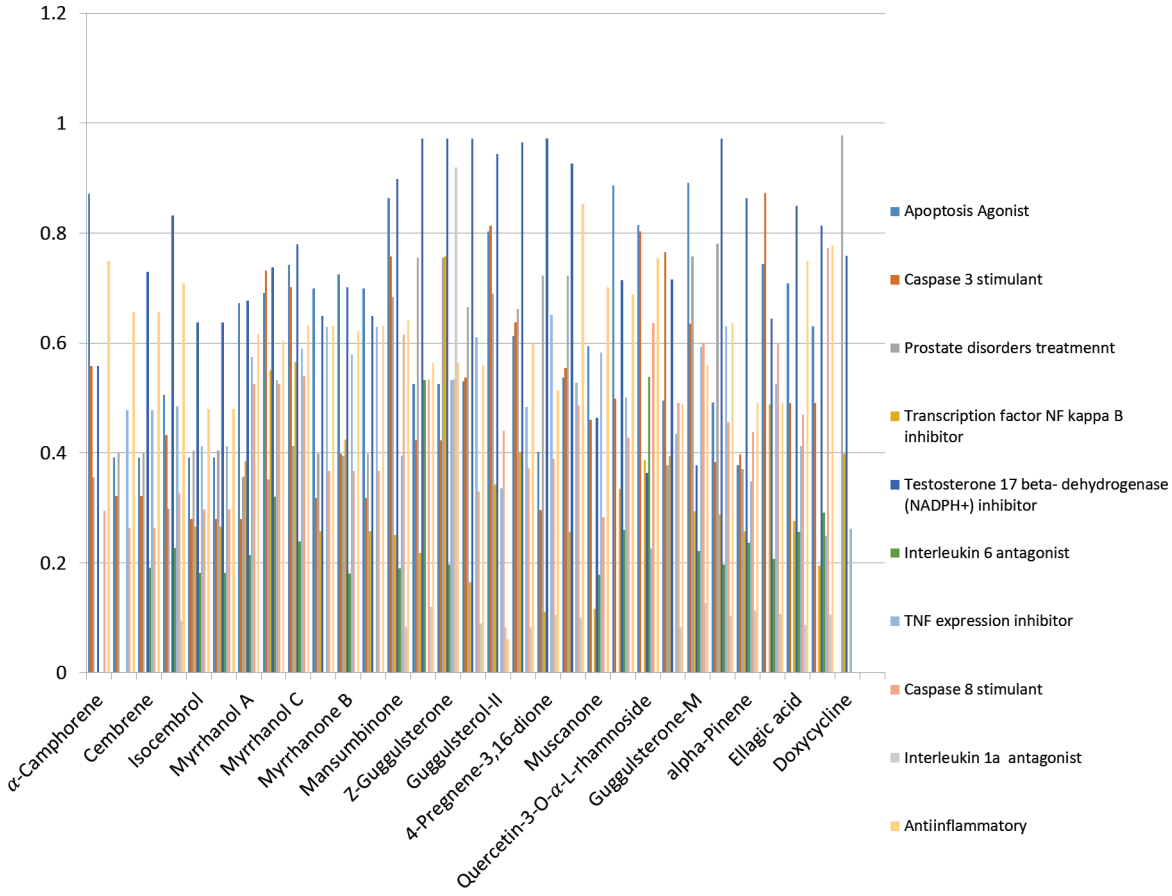


Figure 4. All activities of all compounds concerning Doxycycline.

Table 3. Clinical studies characteristic

Study No.	Author	Study	Subject	Phyto constituent Treatment	Duration	Parameter Evaluated	Odd ratio
1	JAMES ELIST, 2006 (18)	Randomized, Double-Blinded clinical trial	The study was done at Age 18 Years and older	ellagic acid	6 months	NIH-CPSI score	1.4933 (0.5815 to 3.8349)
2	"F. Lombardo, M. Fiducia, R. Lunghi, L. Marchetti, A. Palumbo, F. Rizzo, A. Koverech, A. Lenzi and L. Gandini,2011 "(19)	Randomized, open clinical trial	The study was done at 30 and 55 years	ellagic acid	6 months	NIH-CPSI score	2.3333 (1.0026 to 5.4301)
3	Joyal Patel, Tukaram Dudhamal, 2017 (20)	Randomized, open clinical trial	The study was done at age above 40 years	Z-*Guggul* sterone	30 days	International Prostate Symptom Score (IPSS)	1.0741 (0.0369 to 31.2603)
4	Danish Javed*, Pradeep Kumar, Devesh Shukla, Sana Anwar, Binish Javed, 2015 (21)	Randomized, open clinical trial	The study was done at age above 45 years	Z-*Guggul* sterone	90 days	Modified Boyarsky score and international prostate symptom score	4.8000 (2.1736 to 10.6002)
5	DANIEL A. SHOSKES, SCOTT I. ZEITLIN, ASHA SHAHED, AND JACOB RAJFER,1999 (22)	Randomized, double-blind clinical trial	The study was done at age above 40 years	Quercetin	30 days	NIH symptom score	2.8750 (1.1114 to 7.4372)
6	Angela Maurizi, Francesco De Luca (2018) (23)	Randomized, open clinical trial	The study was done with participants ages above 18 and less than 65 years	Quercetin	21 days- 6 months	NIH symptom score	1.8000 (0.0266 to 21.7123)
7	Patel Joyal, Dudhamal TS, Gupta SK, Mahanta VD, 2014. (24)	Randomized, open clinical trial	The study was done with participants aged above 40 years	Quercetin	21 days	International Prostate Symptom Score (IPSS).	1.1500 (0.5155 to 2.5652

respectively. We can readily deduce from the above-mentioned data that the phytoconstituent had a more substantial effect on the improvement of the "NIH-Chronic Prostatitis Symptom Index (CPSI)" in human participants.

The figure-6depicts the Ors (95% CI) of studies 3 and 4 for decrease in prostate weight with phytoconstituent (Z-*Guggul* sterone) treatment are 1.074 (0.0369 to 31.2603), and 14.8000 (2.1736 to 10.6002) respectively. We can deduce from the above-mentioned data that the phytoconstituent had a considerable influence on the improvement of prostatic weight loss in human individuals.

Figure 7 illustrates the Ors (95% CI) of studies 5 and 6 for Total (NIH SYMPTOM SCORE) with phytoconstituent (Quercetin) treatment are 2.8750 (1.1114 to 7.4372) and OD for NIH- 1.3158 (0.5911 to 2.9291) respectively. We can easily deduce from the above-mentioned Figures that the phytoconstituent had a more substantial influence on the improvement

of Total (NIH SYMPTOM SCORE) in human participants.

Figure 8 illustrates the Ors (95% CI) of studies 7 and 8 for International Prostate Symptom Score (IPSS) with phytoconstituent (Quercetin) treatment are 1.8000 (0.0266 to 21.7123) and 1.1500 (0.5155 to 2.5652) respectively. We can easily deduce from the above-mentioned results that the phytoconstituent had a more substantial influence on the improvement of Total IPSS score in human participants.

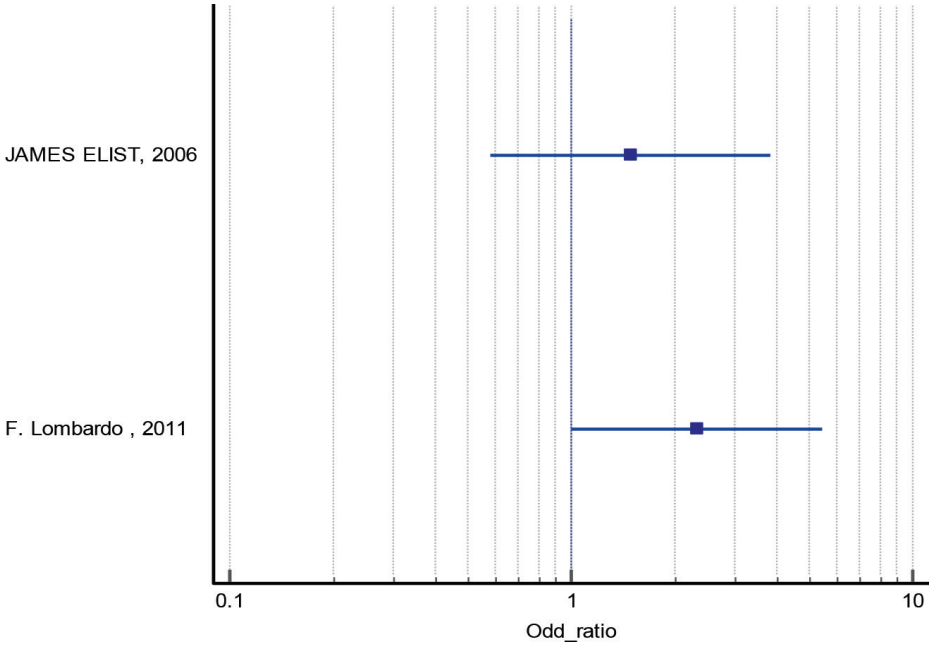


Figure 5. Ors (95% CI) - Chronic Prostatitis Symptom Index (CPSI) with phytoconstituent (ellagic acid).

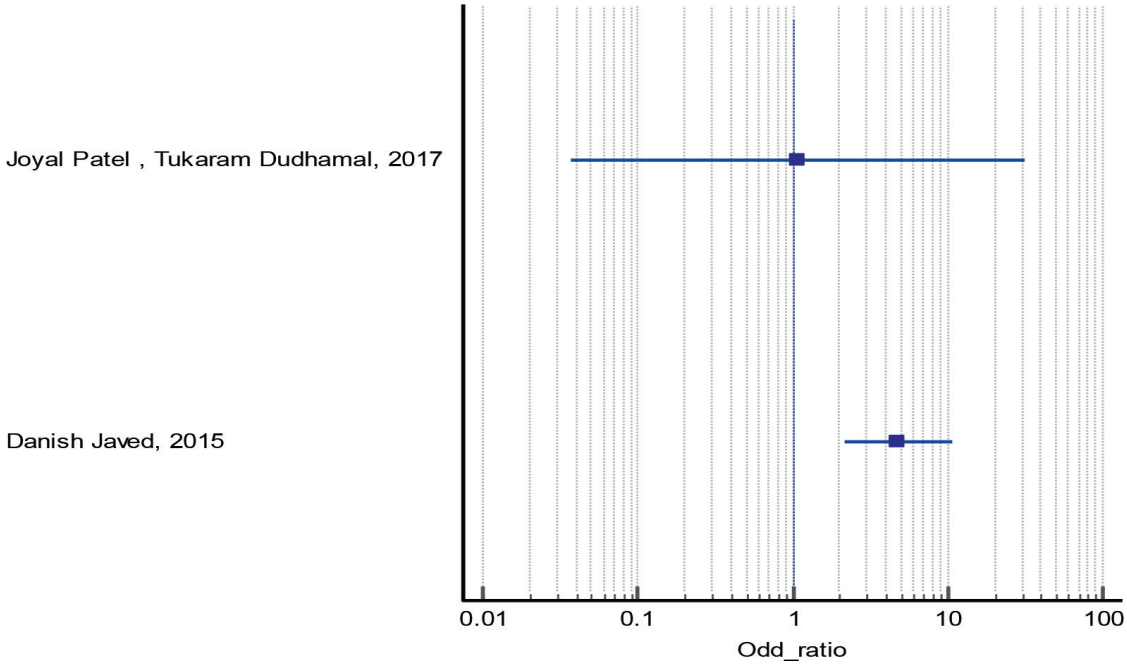


Figure 6. Ors (95% CI) -prostate weight with phytoconstituent (Z-*Guggul* sterone).

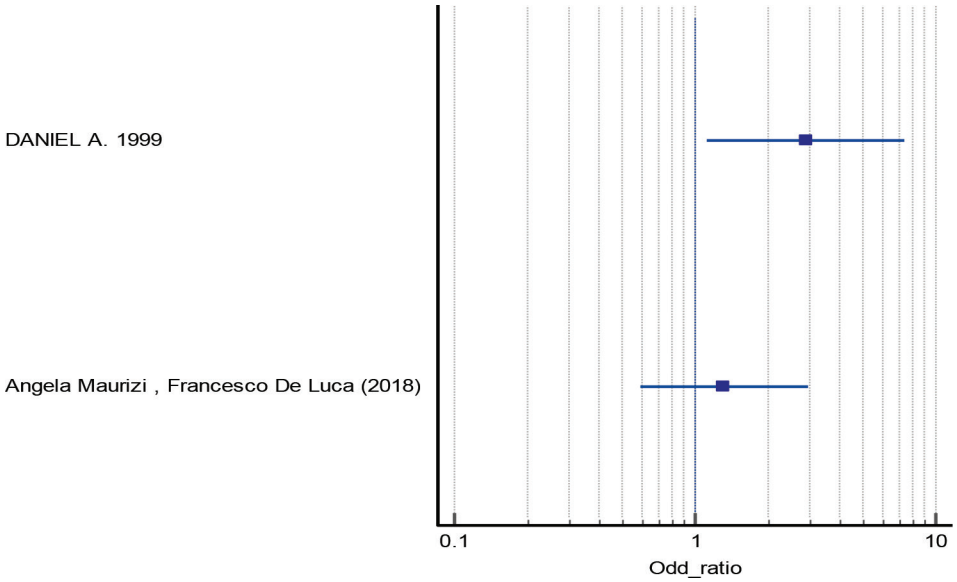


Figure 7. Ors (95% CI) -NIH SYMPTOM SCORE with phytoconstituent (Quercetin).

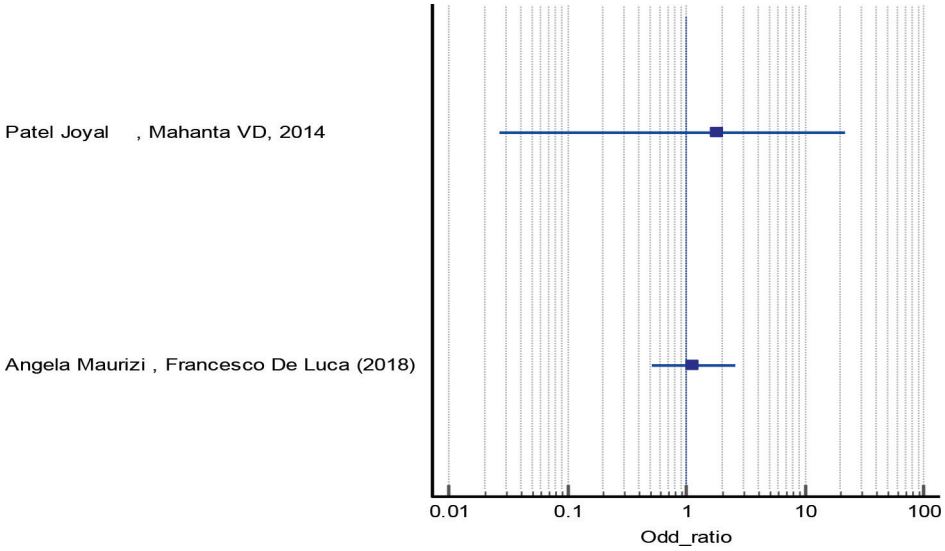


Figure 8. Ors (95% CI) -International Prostate Symptom Score (IPSS) with phytoconstituent (Quercetin).

8. Discussion

Despite an incomplete understanding of the pathophysiology of chronic prostatitis, it is evident that many pathways contribute to the onset and advancement of illness[28-30]. These changes essentially consist of hormonal and circulatory alterations at both the local and systemic levels. Additionally, there is prostatic inflammation that stimulates the proliferation of cells[31-34].

Research indicates that the Prediction of Activity Spectra of Substances (PASS) program offers data that supports the claimed activities of phytoconstituents. This study examined the documented activity of all phytoconstituents and their impact on chronic prostatitis in treating prostate cancer. And also predicted the actions of all phytoconstituents that have the potential to be utilized in the treatment of chronic prostatitis. In this study, the aim of this study is to gather information about the potential anti-chronic prostatitis activity of specific important phytoconstituents. Our findings suggest that *Guggul* sterone-z could be a promising candidate for further investigation in the development of medication therapy for chronic prostatitis. The meta-analysis specifically aims to identify the clinical trial for

the chosen phytoconstituent (listed under clinical trials) for chronic prostatitis. The selected phytoconstituents produced the highest number of results when tested in clinical trials; the phytoconstituent generated the highest number of studies. The Pass prediction findings indicate that *Guggul* sterone Z, followed by Mansumbinone, 16-dehydroprogesterone, and alpha-pinene, exhibit the greatest number of activities. The primary objective of this meta-analysis is to identify clinical studies that specifically involve the selected phytoconstituent for the treatment of chronic prostatitis. From the meta-analysis of clinical studies, it may be deduced that phytoconstituents have positive effects. *Guggul* sterone Z did not have a significant effect on reducing prostate weight in human subjects. However, the phytoconstituent Quercetin did have a significant effect on improving the Total UPDRS score in human subjects, according to two studies with an Odds Ratio (OR) greater than 1. Additionally, the phytoconstituent ellagic acid showed an even more significant effect on improving the NIH-Chronic Prostatitis Symptom Index (CPSI) in two studies with an OR greater than 1. These studies were conducted on patients with chronic prostatitis.

9. Conclusion

The preceding analysis yielded data indicating that the PASS program provided activity information on phytoconstituents. The stated activity of each phytoconstituent is being compared to its supposed effect on chronic prostatitis. Moreover, the potential effects of all phytoconstituents on the therapy of chronic prostatitis were forecasted. The focus of this research is on the anti-chronic prostatitis activity of certain phytoconstituents, as predicted by PASS. Upon isolating diverse phytoconstituents, we have ascertained that *Guggul* sterone Z, Mansumbinone, 16-dehydroprogesterone, and alpha-pinene exhibit potential for additional investigation in the advancement of pharmaceutical treatment for chronic prostatitis. After conducting the meta-analysis, we found that the ODD RATIOS consistently showed that *Guggul* sterone Z, followed by Mansumbinone, 16-dehydroprogesterone, and alpha-pinene, could be potential targets for further research in the development of new therapy for chronic prostatitis. These compounds, in addition to doxycycline, are valuable for targeting various important causes of chronic prostatitis.

Notwithstanding the availability of multiple therapeutic options for cancer patients, the global rate of cancer incidence as well as death is worrying most contemporary cancer treatments include synthetic in origin mono-targeted exceedingly costly and inefficient and they typically have significant adverse effects as a result there exists an urgent requirement to find alternative medications for combating cancer. Further study on *Guggulu* phytoconstituents *in vivo* and *in vitro* studies can be scientifically important evaluative measures needed for further revealing the unexplored therapeutic potential of *Guggulu* for the treatment of prostate cancer.

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