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Global Research Landscape of Natural Medicines for Lower Urinary Tract Symptoms: Bibliometric and Clinical Trial Analysis

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Abstract

Background

Natural medicines have demonstrated significant therapeutic potential in the management and attenuation of lower urinary tract symptoms (LUTS). According to the Web of Science Core Collection (WoSCC), a total of 497 related articles have been published during the last 25 years. China was the most productive country, followed by India and the United States. However, the United States showed substantial influence in earlier years and contributed prominently to clinical trial activity. This study employs a systematic, visualized synthesis of bibliometric and clinical trial data to effectively delineate the research frontier and inform future directions.

Methods

To map the research landscape, a bibliometric examination was performed using a structured search query to gather relevant papers on natural medicines and urinary symptoms published over a 25-year span. The information extracted for analysis included titles, journals, authors, affiliations, citations, keywords, and a set of keywords associated with natural medicines for urinary symptoms. Furthermore, the ClinicalTrials.gov registry was utilized to evaluate the profile of trials testing natural agents against LUTS.

Results

Incorporating 497 publications from 78 nations, this study's bibliometric evaluation accounted for a substantial body of literature that referenced 22,160 individual documents. China produced the highest number of publications. Review of clinical data suggests that trials are predominantly situated in phases II-Ⅲ, and research in this field demonstrates phased growth, with institutional funding continuing to expand.

Conclusion

This analysis has traced research outcomes and transformation models regarding natural medicines in LUTS management. Clinical investigation confirms the field's evolution toward practical implementation. A central goal of present-day investigation involves delineating the pathological mechanisms of LUTS progression, defining particular common signaling routes, and producing effective clinical medications.

1. Introduction

The presenting features of lower urinary tract symptoms often have core components like frequent urination, urgent voiding, and difficulty in passing urine[1]. Lower urinary tract symptoms affect

approximately 2.3 billion individuals worldwide, with a substantial burden among older men. US statistics indicate 13% benign prostatic hyperplasia(BPH) frequency in 40-49-year-olds and 28% LUTS incidence in men over 70. These disorders potentially affect 40% of males beyond 50 years. Nearly 63% of men aged 65 + received BPH medication within 5 years following diagnosis.This symptomatic complex is particularly widespread among elderly males[2], frequently accompanying BPH[3, 4]. The detrimental impact of LUTS on daily life and healthcare costs is well-established[1, 5]. While α1-adrenoceptor antagonists and 5-alpha-reductase inhibitors form the cornerstone of pharmacological management[6, 7], their utility is constrained by untoward effects like erectile dysfunction and blood pressure changes[8], hindering sustained use[9–13]. Therefore, identifying novel and well-tolerated interventions is a pressing clinical priority[14]. Scientific evidence supports the LUTS-alleviating effects of botanical products including saw palmetto, nettle root extracts, and pumpkin seed oil. Traditional Chinese medicinal formulas like Pule'an Tablets and Qianliekang have achieved satisfactory clinical efficacy. Mechanistically, the ability of natural medicines to interact with a network of targets, along with their reduced toxicity, presents an appealing strategy for treating LUTS[15–17]. While the scientific literature concerning natural medicines and LUTS has seen a marked increase in recent years, no study has yet systematically synthesized and visualized the intellectual landscape, including its evolutionary pathways and collaborative structures. Bibliometric analysis provides quantitative evaluation of scholarly works, identifying research formations, evolutionary courses, and emerging fronts in particular domains. The objective of this work is to uncover the knowledge structure and dynamics within the domain of natural medicines for LUTS. By analyzing a corpus of literature from 2000 to 2025 with CiteSpace, we will profile contributions across various levels and visualize networks to highlight future directions for the field[18]. Although laboratory studies show encouraging results, clinical evidence is needed to confirm therapeutic value in patients[19, 20]. Studies of natural medicinal compounds are developing through ongoing scientific investigation and initial clinical testing, while complete bibliometric assessment and comprehensive overviews of current knowledge have not yet been published. Our work establishes the first comprehensive profile of global research output on natural medicines for LUTS. We systematically chart the research territory, identify frontier areas, and trace evolutionary patterns. Clinical trial trends for natural medicines in LUTS were further examined by integrating and visually analyzing data from ClinicalTrials.gov.

2. Materials and methods

2.1 Data source and literature search strategy

Data for our bibliometric analysis were obtained from the WoSCC.. A static bibliometric analysis was performed using publications concerning natural medicines for LUTS retrieved from WoSCC. After implementing a systematic literature retrieval strategy, we assembled a dataset spanning the previous quarter-century. The workflow diagram is shown in Fig. 1. We developed our search methodology based on published reviews (Sava et al., 2020; Li et al., 2022) while incorporating specialist input during literature evaluation. The investigative team unanimously adopted the systematic search approach

utilizing TS=("Nature medicine" OR "nature drug" OR "Traditional Chinese medicine" OR "Chinese medicine" OR "Chinese medicinal formula*" OR "Prescription of traditional Chinese medicine" OR "Herb" OR "Medicinal plant" OR "Herbal medicine" OR "Plant extract" OR "Herb extract*" OR "Herbal compound*" OR "Plant compound*" OR "Phytochemical*") AND ("Chronic prostatitis" OR "Interstitial cystitis" OR "Lower urinary tract symptoms" OR "Lower urinary tract dysfunction" OR "Overactive bladder" OR "Incontinence" OR "Urolithiasis" OR "urinary disorder" OR "Benign prostatic hyperplasia" OR "Benign prostatic enlargement"). All phases of literature identification, data extraction, processing, and downloading were carried out by a single investigator during one session to ensure methodological consistency. A total of 497 scholarly articles and reviews published from 2000 to July 23, 2025, were selected for analysis, with only formal English publications eligible. Comprehensive bibliographic metadata were preserved to prevent inconsistencies during multiple retrieval sessions. The complete WoSCC dataset was exported in plain text format with tab separators.

2.2 Data analysis and graph acquisition

Our methodology applied CiteSpace combined with VOSviewer for bibliometric investigation. The visualization of literature networks employed contemporary R and RStudio versions with integration of bibliometrix (v4.1.4). To delineate research fronts and analyze thematic concentrations, we compiled PubMed data on natural medicinal applications for LUTS. Cross-national cooperation frequencies were visualized utilizing ArcMap (v10.8). We utilized Microsoft Excel 2019 and GraphPad Prism 9.3.1 for data compilation and graphical presentation. Network charts were produced using VOSviewer (version 1.6.20) after data importation. Citation data served as the foundation for network development, enabling exploration of co-authorship patterns, keyword co-occurrences, and citation relationships. A full counting methodology was applied, where each publication was counted once regardless of author count. The VOSviewer application determined publication and citation metrics along with keyword frequencies. Visualization and construction of key term co-occurrence networks were achieved using the software's integrated clustering functionality. Our research emphasizes co-occurrence examination as its fundamental analytical strategy, representing the study's main contribution. This methodology was applied to evaluate collaborative interactions across geographical, institutional, and author levels. The software identifies strongly cited publications and terms showing notable citation acceleration over time.

2.3 Analysis of clinical trials data

Clinical trial registration information was sourced from ClinicalTrials.gov to enable a detailed analysis of natural medicines research progress for LUTS. We implemented a search using the terms "natural medicines," "herbal medicines," "lower urinary tract symptoms," "benign prostatic hyperplasia," and "overactive bladder," which included all publications through July 2025. Extracted details consisted of experimental phase, launch date, investigation design, funding classification, and national dispersion. After arrangement with Microsoft Excel 2019, descriptive analysis and trend commentary were carried

out in conjunction with bibliometric insights, addressing gaps in traditional literature appraisal regarding clinical implementation.

3. Results

3.1. Overview of publication status

The transformation of bibliometric and citation analysis has extended from scientometrics through informetrics to webometrics. Examination of network information allows researchers to comprehend academic linkages and generate plausible predictions about forthcoming scientific endeavors. We carried out a detailed bibliometric assessment of natural medicines for LUTS. Progressive screening criteria included: publication period (2000.01.01-2025.07.23; 526 records), article type (research articles and reviews; 505 records), and language restriction (English; 497 records). We examined 497 scientific works on nature drugs and LUTS published during 2000–2025. Table 1 provides a summary of fundamental information derived from the WoSCC database.

Table 1
The main information of the data

Description	Results
Documents	497
Article	402
Review	95
Time span	2000:2025.7.23
Sources (journals, books, etc.)	239
Annual growth rate (%)	7.97%
Document average age	6.57
References	22160
Average citations per doc	14.36

3.2 Annual publication trends

We characterized publication trends for natural medicines and LUTS by quantifying annual and cumulative publication volumes from 2000 to 2025. As depicted in Fig. 2A, publication output in natural medicines for LUTS demonstrates a consistent upward trajectory. The field recorded 5 publications in 2000 and 7 in 2008, reflecting limited scholarly attention during this initial phase. Subsequent recognition of natural medicines' therapeutic potential stimulated rapid growth over the following 18 years, culminating in 53 publications by 2024. Furthermore, we performed regression fitting on accumulated publication data to establish a predictive formula. The high determination coefficient (R^2 =

0.999) reveals sustained advancement in natural medicines and LUTS investigations. Based on WoSCC records visualized in Fig. 2B, China, the United States, and India lead in natural medicines publications. The research output from these three nations exceeds the aggregate publications from all other countries. Supplementary Table 1 presents the full results. The top-performing institutions included ten Chinese organizations that collectively published 131 natural medicines and LUTS articles. The China Academy of Chinese Medical Sciences maintained leadership with 19 publications (Fig. 2C).

3.3 Analysis of partnerships and cooperation among nations

Through ArcGIS spatial analysis, we mapped publication distribution across 78 countries involved in natural medicines and LUTS investigations (Fig. 3A), showing global research engagement. The global distribution of publications (Fig. 3A) reveals China's dominant position with 252 publications, followed by India (49), the United States (44), South Korea (32), Pakistan (18), and Saudi Arabia. A substantial gap separates these nations from other contributors. Additionally, collaborative networks were visualized through circular charts (Fig. 3B, VOSviewer) and world maps (Fig. 3C, Scimago Graphica). The diagram in Fig. 3B shows countries as circles proportional to their publication numbers. Collaborative relationships strengthen progressively from Croatia culminating at China. India maintains the second-largest global publication output following China. A color gradient from pale green to blue indicates cooperation intensity. China participates significantly among the 78 cooperating nations. Our findings identify China as fundamentally important to natural medicines and LUTS research. This conclusion is consistently supported by VOSviewer data (Supplementary Fig. 1). As illustrated in Fig. 3C, Egypt and Saudi Arabia exhibited the highest collaboration frequency (64 instances). Subsequent partnership counts were observed for China-USA (43), Saudi Arabia-India (39), India-USA (25), Italy-Spain (23), and Saudi Arabia-Pakistan (20). While Egypt-Saudi Arabia collaboration was most frequent, China maintained numerous high-count international partnerships. Supplementary Table 2 presents complete details. National research output across time periods is illustrated in Fig. 3D. Hue progression from dark blue to light yellow signifies temporal sequence. Investigation revealed predominant United States contributions a decade ago, superseded by Chinese research leadership five years back, and currently showing emerging productivity from Egypt and Saudi Arabia. This redistribution may associate with increased recognition of natural medicines' therapeutic relevance. Author distribution analysis demonstrates similar chronological patterns (Supplementary Fig. 2), indicating China's ongoing academic prominence.

3.4 The evolution of research disciplines

Using CiteSpace, we generated a dual-map overlay to characterize the inter-journal citation patterns and their corresponding subject area distributions. On the left side of Fig. 4A, the citing journals are visualized, and the right side presents the distribution of cited journals. Journals are depicted as individual points on the map, the arcs represent citation links, conveying the entirety of the referencing behavior.The thickest curve in Fig. 4A reflects core references pertaining to natural medicines and LUTS,

initially published in molecular, biological, or immunology journals, and subsequently cited most often by journals specializing in molecular and genetic research. This pattern highlights cross-disciplinary interaction within the filed.

3.5 Analysis of cocited references

From the 497 retrieved publications, 15,982 reference citations were extracted. Co-cited references typically constitute the knowledge foundation of a research field. Investigation of citation networks establishes the intellectual background for nature drugs and LUTS research. CiteSpace software generated eleven major clusters employing log-likelihood ratio computation, with clustering based on reference keywords. The identified clusters comprised "symptom relief" (cluster #0, size = 61), "integrative therapy" (#1, 56), "natural drug" (#2, 39), "plant-based therapy" (#3, 37), "chronic pelvic pain syndrome" (#4, 32), "prostatic hyperplasia" (#5, 25), "botanical medicine" (#6, 24), "uvaria rufa blume" (#7, 23), "benign" (#8, 23), "herb-drug interaction" (#9, 22), and "urolithiasis mitigation" (#10, 18). Clusters #5, #8, #4, and #7 address multiple etiologies underlying LUTS. Clusters #9 and #2 represent the varieties and mechanisms of natural medicines cited in LUTS research. Clusters #0, #1, and #3 demonstrate the clinical value and therapeutic potential of natural medicines.

3.6 Analysis of top-cited articles

Bibliometric analysis fundamentally relies on citation assessment, which supports impact factor determination. Works garnering frequent citations are deemed scientifically influential. These highly cited publications establish the conceptual framework that orients scholarly inquiry. The ten most-highly cited publications appear in Table 2, sequenced by decreasing citation frequency. Most of these significant papers were produced between 2014 and 2017. With a combined total of 1,248 citations, these articles exhibited citation counts that ranged from 81 to 161. According to our evaluation, the comprehensive review of parsley's ethnopharmacology, phytochemistry, and biological functions accumulated the highest citation frequency (161), detailing its applications in urological disorders. This demonstrates research emphasis on parsley as a significant medicinal resource with established bioactivities. [21] revealed antibacterial properties in Urtica phytochemicals, permitting their incorporation into functional foods and pharmaceutical products. Forty percent of the top-cited publications addressed ethnomedical knowledge and plant chemistry for therapeutic development.

Table 2
The top 10 papers with the highest number of citations

Rank	Title	Key points	Journal	Local citation	Year
1	Parsley: a review of ethnopharmacology, phytochemistry and biological activities	Parsley has long been used in ethnomedicine for urinary tract conditions, including diuretic, anti-urolithiasis, and antiseptic effects. Active compounds such as apigenin, apiol, and myristicin support its role in managing lower urinary tract symptoms through antioxidant, diuretic, and anti-inflammatory mechanisms. Highlights its potential as a natural therapeutic option for urinary disorders.	Journal of Traditional Chinese Medicine	161	2013
2	Urtica spp.: Ordinary Plants with Extraordinary Properties	Nettle (Urtica spp.) has traditional use in urinary disorders, with root extracts containing sterols and glycosides that may alleviate lower urinary tract symptoms. Rich in polyphenols and anti-inflammatory compounds, nettle demonstrates antimicrobial and diuretic activity, supporting its role as a natural therapy for urinary tract health. Suggests potential for integration into dietary supplements and pharmacological formulations targeting LUTS.	Molecules	150	2018
3	The genus Anemarrhena Bunge: A review on ethnopharmacology, phytochemistry and pharmacology	Anemarrhena asphodeloides, long used in East Asian medicine, contains saponins, flavonoids, and mangiferin with broad pharmacological actions. Extracts demonstrate anti-inflammatory and antimicrobial properties, suggesting	Journal of Ethnopharmacology	140	2014

Rank	Title	Key points	Journal	Local citation	Year
		potential benefit in urinary tract disorders and LUTS management. Further studies are needed to clarify mechanisms and assess clinical efficacy in urological health.			
4	Clinical Evidence of Herb-Drug Interactions: A Systematic Review by the Natural Standard Research Collaboration	This review identifies over 80 herbs with clinically significant drug interactions, including those commonly used for urinary tract and bladder health. Interactions can alter pharmacokinetics or exacerbate adverse effects, raising concerns for patients using herbal therapies for LUTS alongside conventional medications. Emphasizes the need for vigilance in combining natural medicines with prescription drugs to ensure safe management of urinary disorders.	Current Drug Metabolism	140	2008
5	Dietary Plants for the Prevention and Management of Kidney Stones: Preclinical and Clinical Evidence and Molecular Mechanisms	Highlights that dietary plants such as parsley, nettle, pomegranate, and green tea play a preventive role against kidney stones, a major lower urinary tract disorder. Identifies mechanisms including diuretic, antioxidant, and anti-crystallization effects, which support their potential in managing LUTS linked to urolithiasis. Suggests phytophenols like quercetin and curcumin as promising agents requiring further clinical validation.	International Journal of Molecular Sciences	137	2018

Rank	Title	Key points	Journal	Local citation	Year
6	Medicinal herbs: Drugs or dietary supplements?	Emphasizes that standardized herbal extracts may provide consistent pharmacological activity but differ from whole herbs, where multiple active ingredients act together. Notes the importance of rigorous strategies to validate herbal benefits, including those traditionally used for urinary tract and LUTS management. Suggests that both isolated compounds and whole extracts must be studied to ensure safe and effective applications.	Biochemical Pharmacology	118	2000
7	Botanical medicines for the urinary tract	Reviews key botanical medicines for urinary tract health, including parsley, nettle, and goldenrod as diuretics, and cranberry and uva-ursi for urinary antiseptic effects. Highlights saw palmetto, nettle root, and pygeum as effective for benign prostatic hyperplasia-related LUTS. Underscores their traditional use now supported by modern pharmacological studies.	World Journal of Urology	113	2002
8	Prophylaxis of calcium oxalate stones by Herniaria hirsuta on experimentally induced nephrolithiasis in rats	Demonstrates that Herniaria hirsuta decoction prevents calcium oxalate stone formation in an experimental rat model of nephrolithiasis. Reduces kidney crystal deposits and shifts crystalluria toward smaller, less harmful crystals without major urinary biochemical	BJU International	112	2003

Rank	Title	Key points	Journal	Local citation	Year
		changes, suggesting a direct anti-crystallization effect. Supports its traditional use for urinary tract stone prophylaxis.			
9	Nutritional and pharmacological importance of stinging nettle (Urtica dioica L.): A review	Highlights that Urtica dioica (stinging nettle) has nutritional and pharmacological value, with roots traditionally used for urinary problems linked to benign prostatic hyperplasia. Reviews evidence for antioxidant, anti-inflammatory, and antiproliferative effects across plant parts, supporting its role in managing lower urinary tract symptoms and related conditions. Suggests broad therapeutic potential alongside nutritional uses.	Heliyon	96	2022
10	Stinging nettle, Urtica dioica L.: botanical, phytochemical and pharmacological overview	Reviews Urtica dioica (stinging nettle) as both food and medicine, noting its rediscovery for diverse pharmacological effects. Highlights its traditional role in urinary disorders and its broader activities such as immunomodulatory, anti-infective, and anti-inflammatory properties, supporting interest in its use for lower urinary tract symptom management.	Phytochemistry Reviews	81	2020

3.7 Frequency and clustering analysis of keywords

Keywords in scientific articles denote primary focuses, and their co-occurrence accurately reveals prominent research streams. From 2,148 screened terms, 186 attained the necessary co-occurrence frequency (5). Terminology with similar meanings was aggregated. The twenty most frequent terms are presented in Fig. 5A. Among these keywords, "benign prostatic hyperplasia" was the most frequently

used, appearing 150 times. This was followed by "urolithiasis" (N = 82), while "extract" and "oxidative Stress" both appeared 59 times, sharing the third position. The term "cancer" (N = 30) also ranked among the top twenty keywords. Comprehensive data are provided in Supplementary Table 3. The keywords were organized into four thematic clusters based on conceptual relationships (Fig. 5B). Cluster 1 (red) grouped terms describing mechanistic aspects of natural medicines in LUTS, including "in-vitro," "rats," and "urolithiasis." Cluster 2 (green) assembled keywords related to clinical effectiveness evaluation, such as "traditional Chinese medicine(TCM)," "management," and "acupuncture." Cluster 3 (blue) collected terms addressing disease mechanisms and treatment targets in urinary conditions, particularly "benign prostatic hyperplasia," "urinary-tract symptoms," and "inflammation." Cluster 4 (yellow) gathered keywords focusing on pharmacological targets and mechanisms of natural medicines, primarily "extract" and "oxidative stress." Research trends were identified by applying color gradients to 79 keywords according to citation intensity and temporal occurrence. The analytical networks in Figs. 5C (citation overlap) and 5D (temporal co-occurrence) feature nodes representing keywords. Node dimensions indicate term prevalence, with spatial relationships demonstrating connection strength. Figure 5C employs a color gradient where blue indicates minimal and yellow indicates maximal citation frequency. Dominant terms included "medicinal-plants," "aqueous extract," "glycol-induced urolithiasis," and "double blind”. The chronological distribution of keywords is presented in Fig. 5D, with blue representing early terms and yellow indicating recent ones. Preliminary investigations prioritized "in-vivo," "herb," "phytotherapy," and "calcium oxalate." Modern research emphasizes "oxidative stress," "inflammation," "mechanism," "acupuncture," and "antioxidant." The evolving keyword landscape shows advancement from basic cellular research to therapeutic target exploration for natural medicines in LUTS.

3.8 Further analysis of nature medicine

Figure 6A illustrates the keyword burst detection results. Evaluation of the top 15 burst terms with minimum one-year duration demonstrated "calcium oxalate" (2003–2012) attracted the most sustained scholarly attention. Recently emergent keywords encompass "network pharmacology" (2022–2025), "oxidative stress" (2022–2025), "cancer" (2021–2025), and "risk factors" (2020–2025). The trend likely relates to expanding investigations of natural medicine targets for LUTS, forecasting continued concentration on these terms. We developed a lexical visualization of frequent keywords (Fig. 6B) to determine research focus. Analysis shows dominant interest in oxidative pathways and urolithiasis. Journal contributions were examined using VOSviewer (Fig. 6C).

3.9 Clinical evidence from clinicalTrials.gov studies

Based on ClinicalTrials.gov documentation, this study evaluated clinical investigation features of natural medicinal interventions for LUTS. Analysis showed incremental development with heightened activity between 2006 and 2020, then contraction from 2021 onward potentially affected by international health emergencies. Research efforts predominantly target phases II-IV rather than phase I, underscoring increasing concern for enduring treatment benefits and safety documentation in clinical development (Fig. 7A). Financial support primarily comes from corporate players (excluding large drug firms) and

academic establishments, with cooperative networks exercising important influence. This varied funding ecosystem promotes scientific development while potentially focusing on easily commercialized outcomes(Fig. 7B).The United States and China emerge as principal clinical trial contributors, mirroring their considerable research expenditures in complementary and alternative medicine and deep-rooted traditional medication systems. Italian, Canadian, and other developed nation participation signals accommodating regulatory policies for botanical preparations(Fig. 7C). The most frequent interventions comprise plant-based extracts, nutritional supplements, and redox/anti-inflammatory agents, consistent with traditional remedies' widespread employment in urinary symptom management(Fig. 7D). However, present clinical trials often reveal deficiencies such as limited cohort dimensions and marked methodological inconsistency, undermining conclusions and their translational potential.

4. Discussion

4.1 General information

This study evaluated 497 WoSCC records related to natural medicines in LUTS management. Employing bibliometric R software, VOSviewer, and CiteSpace, we executed detailed examinations of country contributions, organizational partnerships, periodical sources, collaborative networks, and keyword occurrences. Our research also assessed the discipline's conceptual architecture, active research areas, and developmental patterns. The outcomes offer essential groundwork for advancing natural medicine applications in LUTS therapy. Development of medical research and clinical trials necessitates enhanced understanding of natural medicines' contributions to LUTS management[9, 12]. Our investigation represents the first bibliometric examination of natural medicines in LUTS therapy patterns[22–24] across 2000–2025. Growing interest in their therapeutic advantages and clinical outcomes[11, 19, 25] has significantly influenced the research field's expansion. Natural medicines' documented capacity to counter oxidative stress and control inflammatory [26]processes rationalizes the increasing publication volume.

4.2 Analysis of leading countries and institutions

The evolution of natural medicine and LUTS investigations unfolded in two phases. Initial slow progression characterized the pre-2015 period, despite 22 studies appearing in 2014. Following this, the field entered a rapid growth phase where yearly publication counts surpassed 20 from 2016 onward (except 2017). By 2024, annual output peaked at 53 articles, marking substantial advancement in this research area. China and India produced the most substantial publication numbers in natural medicine and LUTS literature. Parallel to country-level patterns, six leading Chinese institutions each generated more than ten articles. The top-ten institutional list featured five Chinese universities. The predominant collaborative format involved international alliances with Chinese participation. These findings recognize China's important role and advanced position in natural medicine research, underpinned by economic resources and scientific investments. Widespread international collaboration would improve overall

research quality. China, Pakistan, and Saudi Arabia reveal substantially growing publication outputs, potentially resulting from expanding geriatric communities.

4.3 Hotspots and trends

Initial scholarly work predominantly focused on treatment efficacy and symptom management through natural preparations including saw palmetto and nettle root extracts for urinary symptoms. Modern scientific approaches have evolved toward mechanism exploration, specifically examining oxidative stress regulation, anti-inflammatory mechanisms, and proliferation modulation such as prostate cell hyperplasia suppression. Increasing prevalence of terms like "oxidative stress," "inflammation," and "mechanism" mirrors scientific progression toward molecular-level understanding of natural medicines' modes of action. Global scientific community has shown expanding interest in Chinese compound formulas and traditional preparations from India and Africa. Research efforts verify clinical benefits while applying network pharmacology and compositional studies to expound multi-target therapeutic approaches, bridging traditional experiences with modern medical evidence. Early vocabulary such as "in-vivo," "rats," and "calcium oxalate" demonstrates original emphasis on animal-based research and experimental models. Current research methodologies reveal expanded application of randomized controlled trials, meta-analyses, and real-world evidence, yielding improved study designs and evidentiary hierarchy. The increasing emphasis on terms including "double blind," "clinical trial," and "management" indicates advancement from basic investigation toward clinical translation. With population aging and rising cancer prevalence, natural medicines gain prominence for managing prostate cancer-associated voiding symptoms, overactive bladder, and calculus prevention. Moreover, medicinal-edible botanicals such as parsley and pumpkin seeds demonstrate emerging utilization in health-functional foods and dietary supplements, providing integrated prophylactic and therapeutic actions. Research leadership is maintained by China, the US, and India, while Egypt and Saudi Arabia demonstrate substantial growth in international alliances, reflecting the domain's global expansion. Multidisciplinary cooperation is particularly visible, merging fundamental medical research, drug discovery, nutrition studies, and computational methods to drive natural medicine exploration toward integrated and precision-oriented approaches.

4.4 Mechanism of natural drug in LUTS

As shown in Fig. 8, natural medicines improve LUTS via multi-target mechanisms[15, 27–32, CHEN & LEE 33], revealing defined developmental stages across 25 years. Scientific inquiry transitioned from observational approaches to mechanistic studies, evolving from single botanical uses to integrated system methodologies. The pre-2015 era primarily emphasized clinical efficacy confirmation and principal bioactive compound identification. Regarding BPH, Saw Palmetto[34–38] and Pygeum africanum[34, 39, 40] attracted maximum research attention, working through 5α-reductase activity suppression and DHT production decrease.

Progress in molecular biological techniques and multi-omics platforms has enabled sophisticated mechanism studies. In benign prostatic hyperplasia, natural medicines including nettle root[41, 42] and

pumpkin seed [43, 44]extracts mediate Nrf2/HO-1 and NF-κB pathway modulation, effectively countering oxidative stress and inflammatory processes independent of classical hormonal mechanisms[45–51]. For neurogenic bladder, capsaicin analogs desensitize TRPV1 to normalize sensation[52, 53]. Fibrosis is countered by astragalus polysaccharide and tetramethylpyrazine through TGF-β1/Smad downregulation[54, 55]. Resveratrol and curcumin promote Nrf2 activity, mitigating oxidative damage to neural and muscular structures[56, 57]. CP/CPPS investigations employing systems pharmacology reveal multi-target actions of herbal[58–61] formulations on cytokine networks including TNF-α and IL-6. Research on overactive bladder increasingly concentrates on TRP channel regulation and sensory nerve sensitization[62–67]. Polyphenolic compounds and terpenoids[68] improve overactive bladder symptoms via anti-inflammatory properties, C-fiber afferent regulation, and acetylcholine release suppression[68–74].

Recent scientific exploration has extended to natural medicines' neuromodulatory and muscular mechanisms in LUTS pathology. Berbamine administration counteracted c-Fos upregulation from retinoic acid exposure while decreasing TRPV1 expression in urinary epithelium[75]. Alpinia oxyphylla extract mediated PKA pathway activation to promote detrusor relaxation, consequently augmenting bladder capacity[76]. Berbamine therapy significantly reduced NGF and BDNF(Brain-Derived Neurotrophic Factor) levels in urine, neurotrophins connected to bladder hypersensitivity and involuntary contractions[75].

Specific natural medicines including rosmarinic acid and ellagic acid demonstrate calcium[77–80] oxalate crystallization inhibition and urinary pH adjustment properties, supporting their adjunct administration for urolithiasis. Innovative approaches such as network pharmacology and metabolomics are promoting an evolution from single-agent single-target research toward multi-component multi-pathway systematic investigations.

4.5 Natural Medicines in the Treatment of LUTS: AI and Multi-Omics Research

Advancing studies of natural medicines for LUTS have highlighted the significant roles of artificial intelligence combined with multi-omics strategies. Early multi-omics development periods featured research that mainly applied genomic and proteomic methodologies for basic target recognition of botanical medicines[81, 82]. Proteomic studies reveal that nettle root preparations mediate anti-inflammatory responses through proteins including COX-2 and iNOS[41, 42, 83, 84]. With progressive accumulation of multi-omics data from transcriptional, metabolic, and protein analyses, network pharmacology has become a significant research emphasis. Through component-target-pathway network modeling, research has thoroughly explained TCM formulas' multi-target modulation of signaling pathways associated with inflammation, oxidative damage, and apoptosis[15, 16, 33, 39, 58]. Multi-platform omics enable prediction of natural medicine component interactions with LUTS targets. Artificial intelligence screening detects plant-derived compounds with 5α-reductase inhibitory activity[85]. Deep learning integration with multi-omics[86] represents a growing research focus in LUTS.

Metabolomic and transcriptomic data fusion with Mendelian randomization reveals BPH pathological pathways and therapeutic targets. CP/CPPS treatment personalization utilizes predictive frameworks combining omics information with clinical metrics[87].

5. Limitations

This study examines the current status of natural medicine in managing LUTS, offering guidance for future research. This research is subject to certain constraints. Primarily, the literature search was confined to publications in English within the WoSCC database. Moreover, trial records obtained from ClinicalTrials.gov were limited to those with a finalized status. Furthermore, delayed recognition due to citation indexing might overlook significant recent publications; thus, these works warrant consideration in subsequent research. The study's temporal focus was further limited to publications from the previous 25 years. We therefore suggest that newly published evidence after July 2025 be analyzed in follow-up work.

6. Conclusions

This investigation delineates the global research trajectory of natural medicines for LUTS between 2000 and 2025, employing bibliometric and clinical registry analyses. The scholarly emphasis has transitioned from preliminary compound isolation to systematic inquiry into multi-target mechanisms, enabled by advances in network pharmacology and omics technologies. Nevertheless, progress is hindered by a paucity of high-caliber randomized trials with extended follow-up and inadequate standardization in quality assessment. Subsequent research ought to establish uniform assessment frameworks for botanical products and implement extensive multicenter studies. These steps will facilitate the transition of natural remedies from supportive care toward precision therapeutic interventions.

Abbreviations

BPH
benign prostatic hyperplasia
BDNF
Brain-Derived Neurotrophic Factor
CP/CPPS
Chronic Prostatitis/Chronic Pelvic Pain Syndrome
C-fiber
C-type nerve fiber
c-Fos
cellular Fos
COX-2
Cyclooxygenase-2
DHT

Dihydrotestosterone
iNOS
Inducible Nitric Oxide Synthase
LUTS
lower urinary tract symptoms
Nrf2
Nuclear factor erythroid 2-related factor 2
NF-κB
Nuclear Factor kappa-light-chain-enhancer of activated B cells
NGF
Nerve Growth Factor
PKA
Protein Kinase A
TRPV1
Transient Receptor Potential Vanilloid 1
TGF-β1
Transforming Growth Factor-beta 1
TNF-α
Tumor Necrosis Factor-alpha
TRP
Transient Receptor Potential
TCM
Traditional Chinese Medicine
WoSCC
Web of Science Core Collection

Declarations

Ethics approval and consent to participate:

Not applicable. This study utilized publicly available bibliographic and registry data; therefore, ethics approval and patient consent were not required.

Authorship Consent for publication: Not applicable

Availability of data and materials: The datasets generated and analyzed during the current study are available in the Web of Science Core Collection and ClinicalTrials.gov repositories. Raw data files are available from the corresponding author upon reasonable request.

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Authors' contributions: QX: Writing – original draft, Methodology, Investigation, Data curation. **QD:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **YY:** Writing – review & editing, Supervision, Funding acquisition, Software, Conceptualization. **LC:** Methodology, Funding acquisition. **JY:** Data curation

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Figures

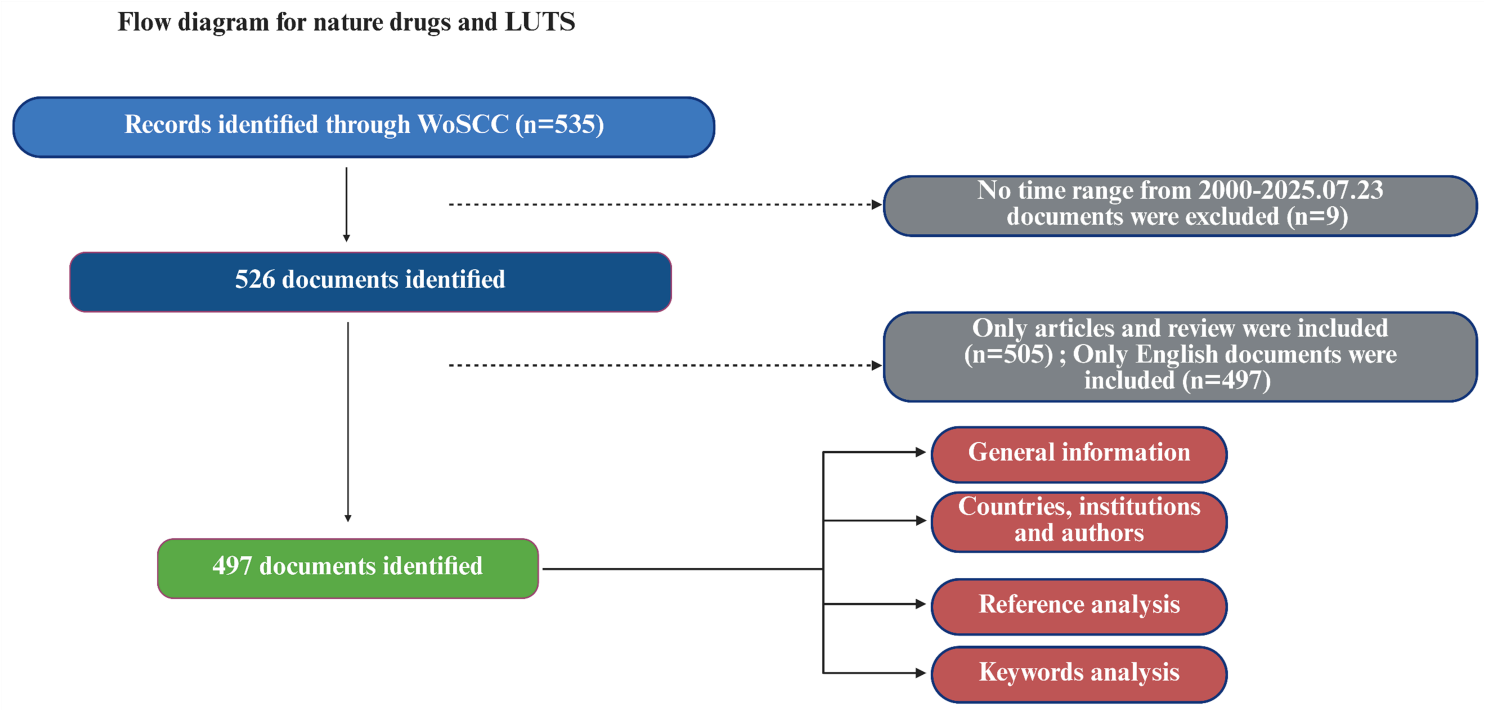


Figure 1

Schematic representation of the workflow used in this study.

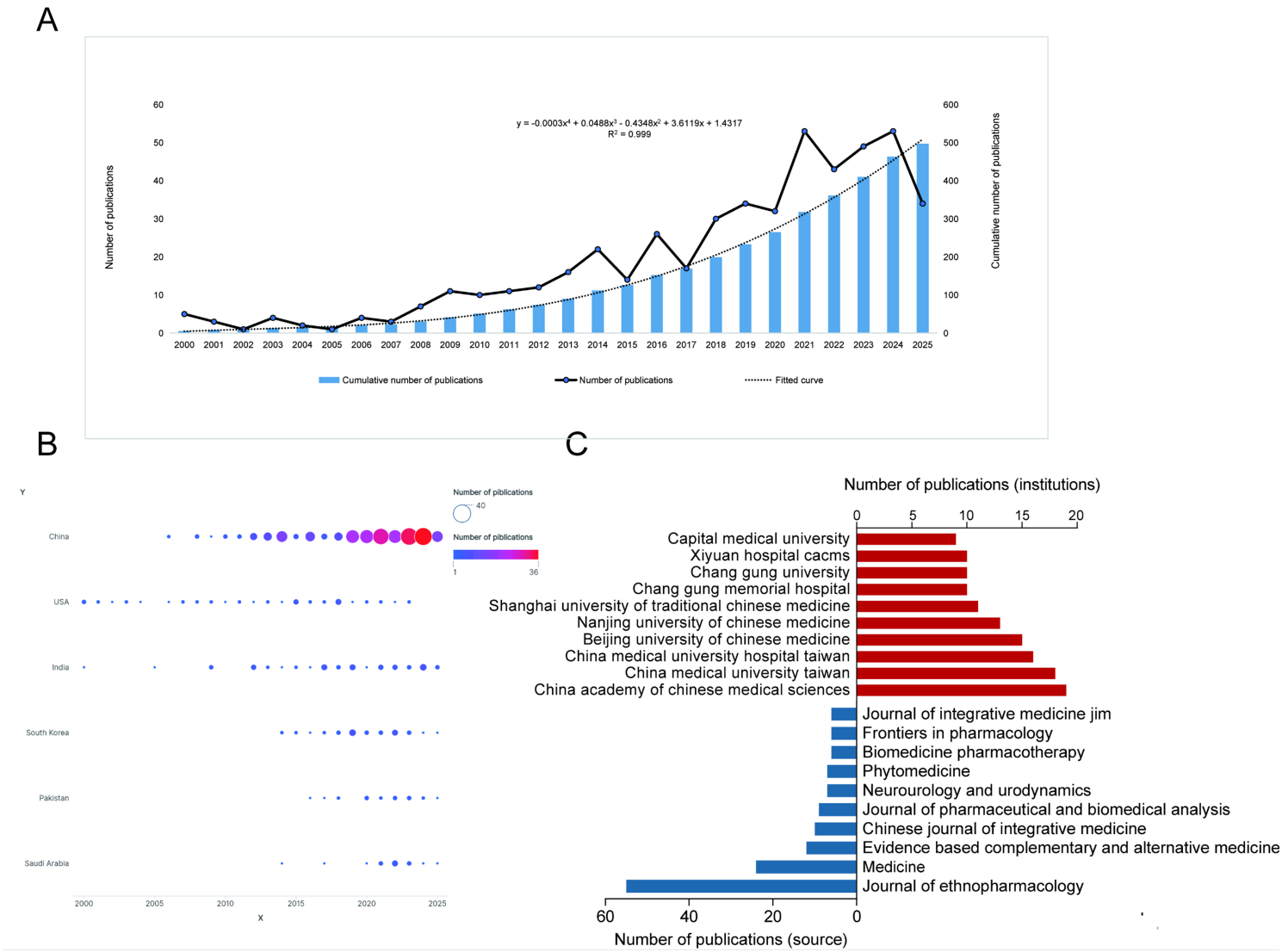


Figure 2

Quantitative review of publication data.**(A)** Trends in natural medicine and LUTS literature output from 2000 to 2025. **(B)** Top ten nations in natural medicine and LUTS scholarly work. **(C)** Leading institutions in natural medicine research for lower urinary tract symptoms.

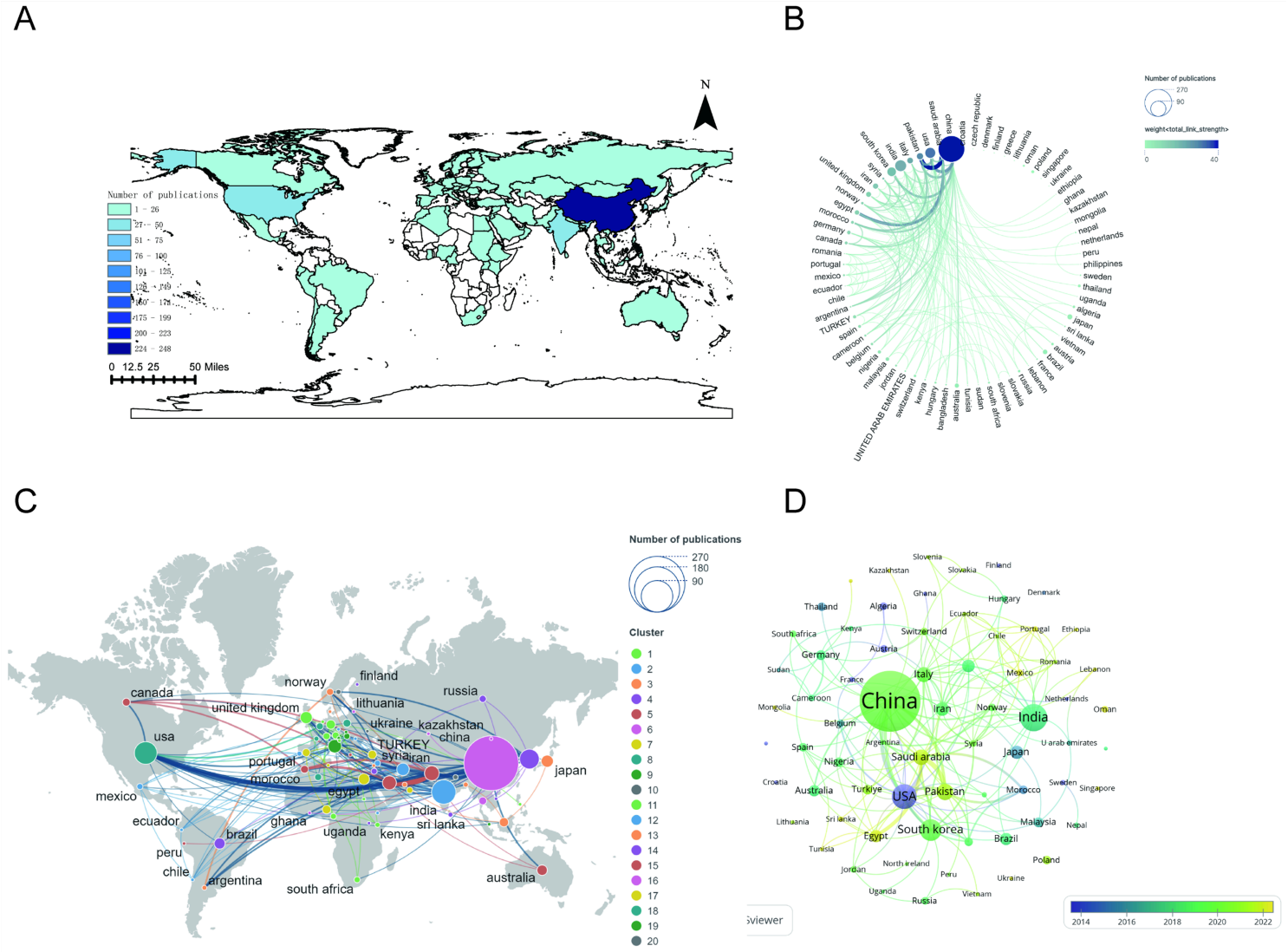


Figure 3

Analysis of cross-national research partnerships. **(A)** World map depicting the contribution of 78 countries to natural product and LUTS investigations. **(B)**Publication count and collaboration network density in natural medicine and LUTS research across 78 nations. **(C)** Country-level citation frequency and number of research alliances in the field of herbal medicine and LUTS. **(D)**Trends in international collaboration (2000–2025).

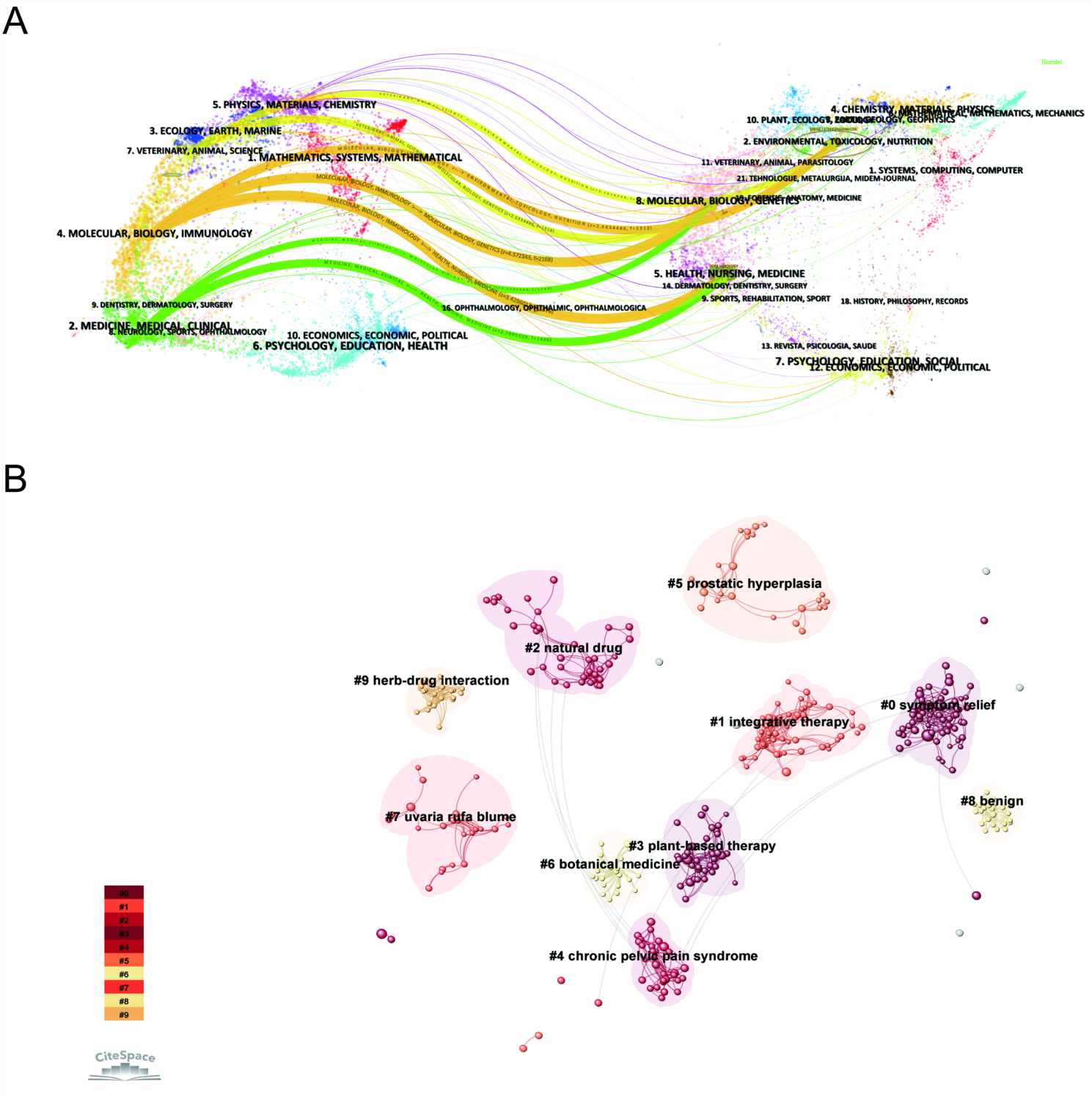


Figure 4

Evolutionary trends in research fields and co-citation networks. **(A)** Dual-map overlay illustrating linked research fields. The left map shows citing publications, the right map cited publications; colored arcs represent knowledge transfer.**(B)** Clustered groups derived from co-citation network analysis.

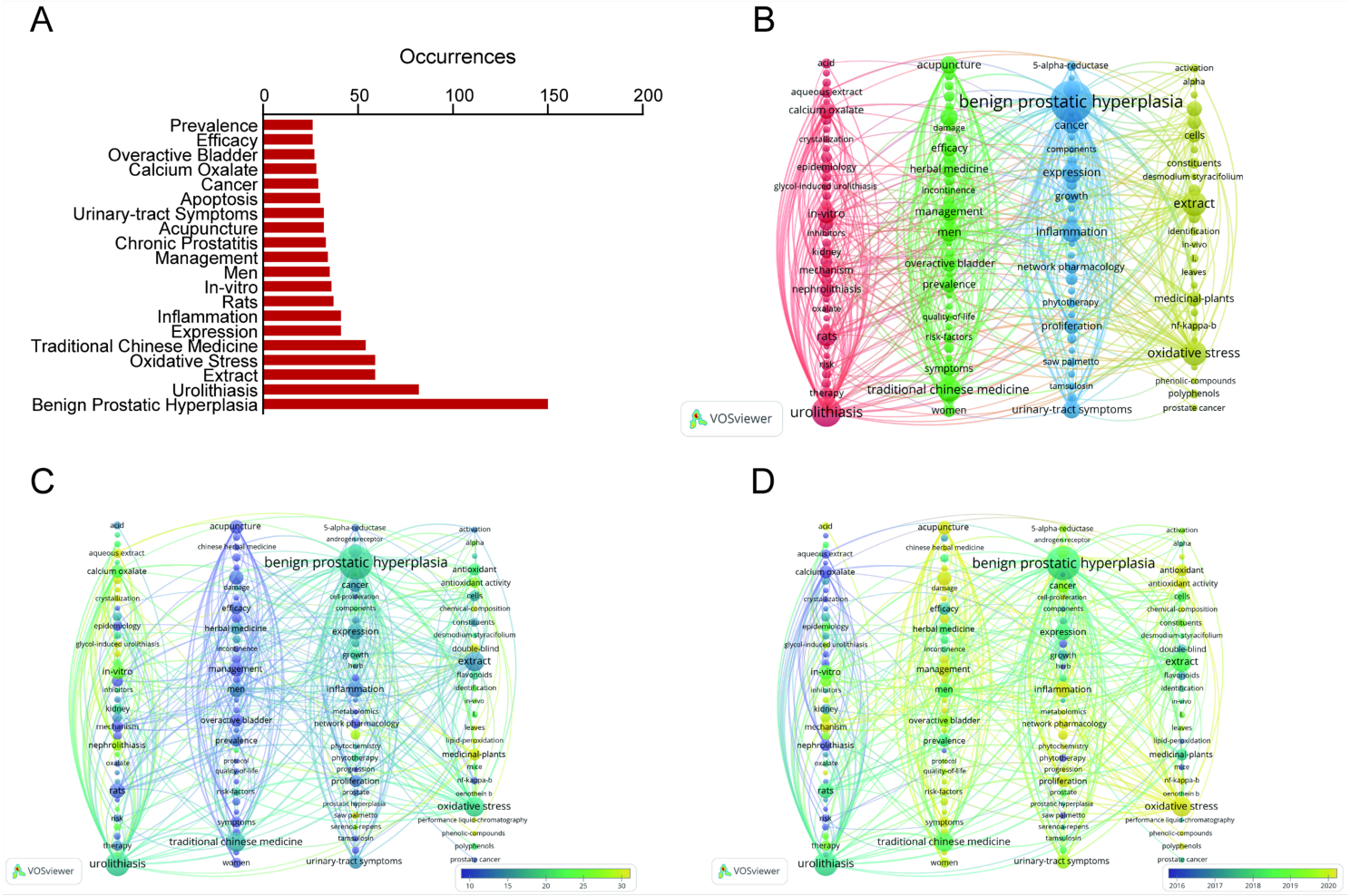
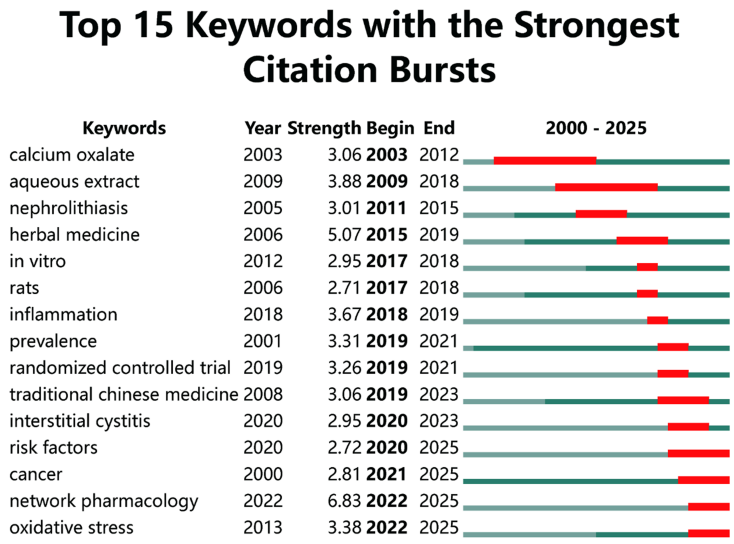


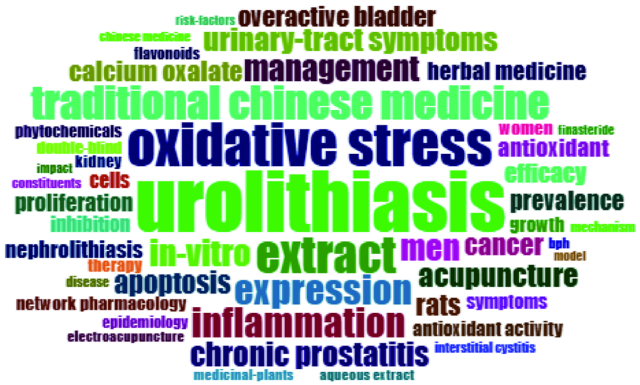
Figure 5

Mapping of thematic keyword connections in natural medicine and urinary symptom research (2000–2025). **(A)** Prominent keywords in research related to natural medicine and LUTS. **(B)** Network-based keyword clustering. **(C)** Network analysis of natural product and LUTS research interconnections. **(D)** Temporal dynamics within keyword relationship networks.

A



B



C

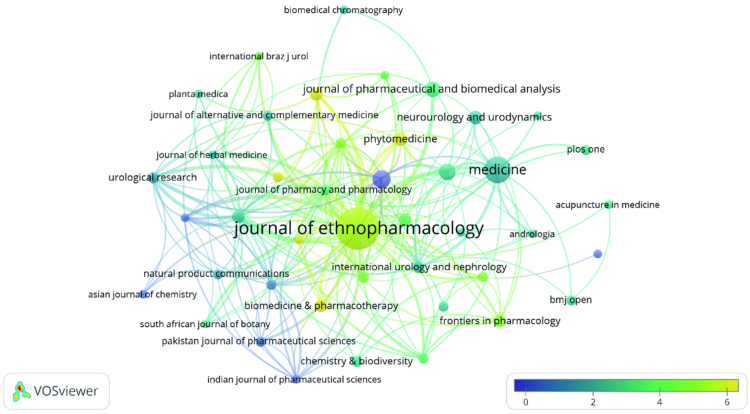


Figure 6

Further exploration of natural treatments for urinary system disorders. **(A)** Ranking of the 15 keywords with the most pronounced citation bursts. **(B)** Word cloud illustrating key terms appearing in literature on natural medicine and LUTS. **(C)** Journal landscape overview for natural medicine and LUTS research.

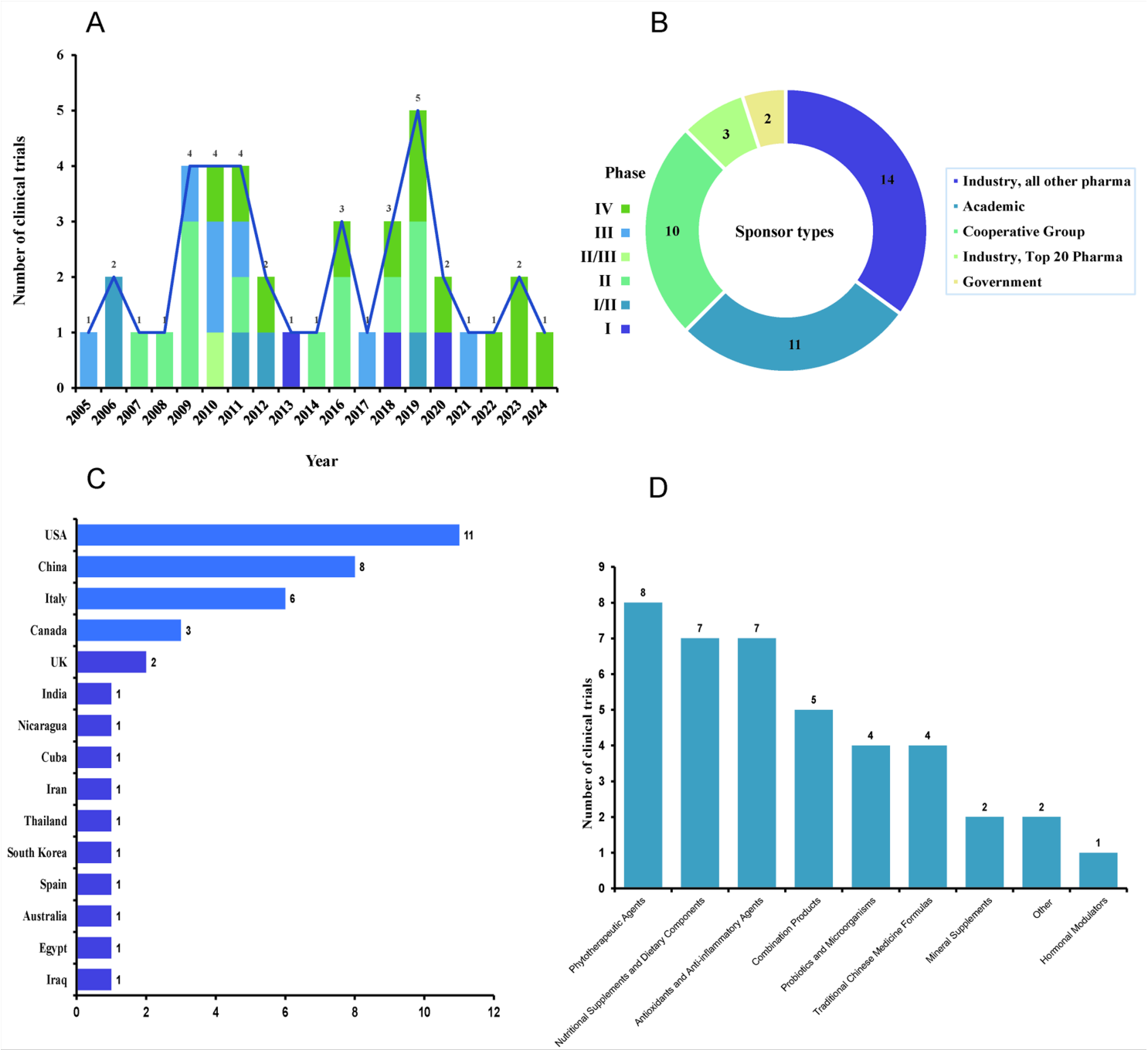


Figure 7

Analysis of registered clinical trials on natural medicines for lower urinary tract symptoms. **(A)** Annual distribution of clinical trials from 2005 to 2024.**(B)** Clinical trial phases (left) and distribution of sponsor categories (right). **(C)** Contribution of leading countries to clinical trial numbers. **(D)** Distribution of clinical trials by intervention type.

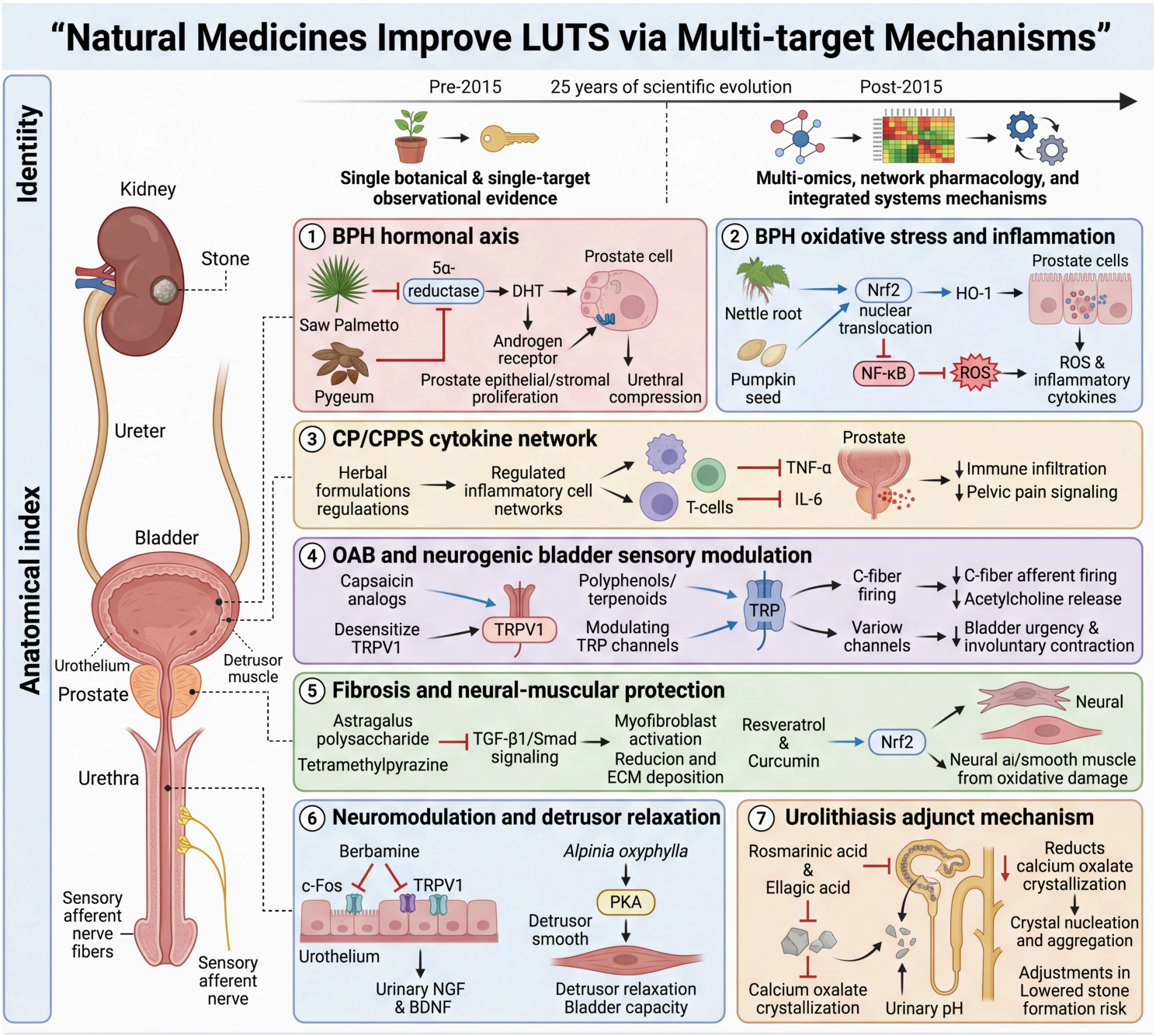


Figure 8

Mechanism of natural medicines in LUTS

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