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SYNERGISTIC SUPPOSITORY HERBAL FORMULATION FOR PROSTATITIS TREATMENT

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Background. Global data indicates that the prevalence of prostate diseases, including prostatitis, ranges from 11% to 74% in men aged 20-65 years. There are clearly defined standards for both conservative and surgical treatment of prostate disease. However, conservative medical treatment of prostatitis does not always allow for a sufficient duration (6-8 weeks) due to the potential for adverse effects. It is currently evident that there is a necessity for the development of products that are highly efficacious with optimal safety profiles, which could ensure their long-term, painless use. In light of the aforementioned considerations, the development of novel multicomponent phytoproducts that exert a direct influence on the functional state of the prostate gland represents a highly promising avenue of research.
Objective. A theoretical study was conducted to investigate the potential synergistic effects of a herbal combination comprising CO_2 extracts of *Serenoa repens*, *Calendula officinalis* and *Levisticum officinale* in the treatment of prostatitis.
Methods. A review of scientific studies conducted by researchers from various countries, as well as an analysis of internationally recognised monographs on phyto-ingredients with established therapeutic properties in the treatment of prostatitis, was undertaken. The data from scientific sources on the potential combination and attainment of favourable synergy for CO_2 extracts of medicinal lovage (*Levisticum officinale*), saw palmetto (*Serenoa repens*) and medicinal calendula (*Calendula officinalis*) were subjected to analysis.
Results. The selection of each herbal extract was based on its distinctive therapeutic properties and the potential for it to complement the others. The saw palmetto (*Serenoa repens*) has been demonstrated to possess anti-inflammatory and anti-androgenic effects, which may be beneficial in the treatment of prostate inflammation and enlargement. Calendula (*Calendula officinalis*) has been demonstrated to possess anti-inflammatory, antimicrobial and wound-healing properties, thereby facilitating the reduction of inflammation and the repair of tissue. Lovage (*Levisticum officinale*) has anti-inflammatory and diuretic properties, which contribute to the reduction of inflammation and improvement in urinary function.
Conclusions. It is anticipated that the theoretical synergy of the studied extracts will enhance the overall therapeutic efficacy, providing improved symptom relief, infection control and tissue regeneration in comparison to traditional treatments. It is anticipated that the suppository delivery system will facilitate localised action with a concomitant reduction in systemic side effects. The proposed formula has the potential to serve as an additional or alternative treatment for prostatitis, pending further experimental validation and clinical trials.

Keywords: Prostatitis, Prostate Protector, Herbal Ingredients, Saw Palmetto, Calendula Officinalis, Levisticum Officinale, Synergistic Formulation, Clinical Evaluation

I. INTRODUCTION

Prostatitis, a complex and often debilitating condition, presents a significant challenge in men's health, affecting millions worldwide [1-3]. Characterized by inflammation of the prostate gland, prostatitis manifests in various forms, from acute bacterial infections to chronic pelvic pain syndromes, each contributing to a spectrum of symptoms that can severely impact a patient's quality of life [4]. Despite advances in medical science, the multifaceted nature of prostatitis continues to elude straightforward treatment, with conventional therapies often falling short in providing sustained relief [5-7].

Conventional therapies often include antibiotics (fluoroquinolones, trimethoprim-sulfamethoxazole, oxazolidinones, macrolides, fosfomycin and others, depending on severity of infection), anti-inflammatory agents and pain relievers (NSAIDs), alpha-blockers (derivatives of piperazine and quinazoline, derivatives of sulfamoylphenethylamine, steroid-like drugs) [8-10]. However, these treatments frequently result in limited success and can lead to undesirable side effects, such as gastrointestinal disturbances [11] and antibiotic resistance [12, 13]. Additionally, the complex and multifactorial nature of prostatitis, which may involve bacterial infection, autoimmunity,

and neurological factors, complicates the therapeutic approach.

In this landscape of persistent clinical need, the exploration of alternative therapeutic avenues has gained momentum [14].

Herbal medicine, with its deep-rooted traditions and growing evidence base, are considered beneficial due to their potential anti-inflammatory, antimicrobial, and immunomodulatory properties, emerges as a promising frontier in the quest for more effective prostatitis treatments [15-17]. Furthermore, the use of herbal medicine is often associated with fewer side effects and a lower risk of drug resistance [18, 19].

It is often accompanied with physiotherapy [20] and acupuncture [21] more efficacies for chronic form.

Among the myriad of botanical options, the saw palmetto stands out for its potent bioactive profile and historical usage in addressing urogenital disorders [22, 23].

In this context, the development of a synergistic herbal suppository formulation represents a promising alternative therapy for prostatitis. By selecting specific herbs known for their therapeutic properties and combining them in a way that enhances their individual effects, this approach aims to provide a more effective and holistic treatment option for managing prostatitis.

By focusing on synergistic interactions, this work seeks to demonstrate that the combined effect of these herbal extracts could be greater than the sum of their individual effects, potentially offering a more effective treatment for prostatitis. The suppository form is chosen for its ability to deliver these active compounds directly to the affected area, improving bioavailability and ensuring targeted action, which could lead to faster and more sustained symptom relief.

The analysis within this article is intended to establish a foundation for understanding the proposed formulation's mechanisms of action and its potential advantages over conventional therapies. While empirical data and clinical trial results are not included, the theoretical perspectives offered here serve to justify further investigation.

Ultimately, the theoretical framework is designed to provide a foundation for future research, offering a rationale for the development of a new class of treatments that could overcome the challenges associated with conventional prostatitis therapies. By highlighting the potential benefits, such as reduced side effects, lower risk of drug resistance, and improved patient outcomes, this framework underscores the need for continued exploration of herbal medicine as a viable alternative in the management of prostatitis.

II. HERBAL INGREDIENTS SELECTION AND JUSTIFICATION FOR SUPPOSITORY HERBAL FORMULATION

A lot of different herbals are used for rectal suppository formulations. Here are some of them (Table 1).

***Table 1*. Herbals used for rectal suppository formulations for prostatitis treatment**

Herb	Form	Bioactive components	Key mechanism	Literature
Serenoa repens	Lipophillic extract	Various phytosterols, free fatty acids (caprylic, capric, lauric, myristic, palmitic, steatic, oleic, linoleic, and linolenic acids) and tocopherols	Inhibition of 5α-Reductase, decreasing the production of dihydrotestosterone (DHT); inhibiting cyclooxygenase (COX) and 5-lipoxygenase (5-LOX) pathways; inhibit the proliferation of epithelial cells in the prostate; modulates autonomic receptors in the lower urinary tract; promotes apoptosis in prostate cells.	[17, 24-30]

Glycyrrhiza glabra	Extract (ethanol)	dipotassium glycyrrhizinate	Inhibition of 11β-HSDs: increases the levels of active cortisol in the body; Impact on Other Enzymes involved in corticosteroid metabolism, further modulating the body's response to stress and inflammation.	[31, 32]
Melaleuca alternifolia	Essential oil	Terpinen-4-ol, γ-terpinene, α-terpinene, α-pinene, 1,8 cineole and linalool	Induction of Apoptosis in PC-3 prostate cancer cells; Disruption of cancer Cell Membranes cell; - increases oxidative stress within the cancer cells.	[31, 33, 34]
Cucurbita pepo	Seeds oil extract	Phytosterols, fatty acids (oleic acids, palmitic acid, linoleic acid), triterpene, and tocopherols	Inhibition of 5-α-Reductase; Inhibition of Proliferation of prostate cancer cells, particularly in PC-3 androgen-insensitive prostate cancer cells; Induction of Autophagy in these cancer cells	[25, 35, 36]
Centella asiatica	Oil extract	Asiatic acid, asiaticoside, madecassic acid, madecassoside, gallic acid, quinic acid, chlorogenic acids, catechin, quercetin and kaempfero	Inhibition of the androgen receptor and PI3K/Akt pathways; Inhibition of human prostate cancer cell metastasis through suppression of the MEK3/6-p38/MAPK signaling pathway via destruction of the MZF-1 and Elk-1 binding interaction	[37-40]
Boswellia serrata	Resin extract (or olibanum)	Boswellic acid derivatives	Inhibition of the 5-lipoxygenase enzyme, inhibition of STAT 3 and Akt in prostate cancer cells; inhibition of androgen receptor by interference of Sp1 binding activity in prostate cancer cells	[41-46]
Helichrysum italicum	Oil extract, essential oil	Sesquiterpenoids (α-cedrene, α-curcumene, geranyl acetate, limonene, nerol, neryl acetate and α-pinene)	Anti-biofilm properties against *Pseudomonas aeruginosa*	[35, 47-51]
Pygeum africanum (Prunus africana or Rosaceae)	extract from the bark (ethanol)	β-sitosterol, β-sitostenone, daucosterol, free fatty acids (lauric, myristic acids), n-docosanol, ferulic acid, ursolic acid	Inhibition of the growth of PC-3 and LNCaP cells; induction of apoptosis and altered cell kinetics; down regulated ERalpha and PKC-alpha protein; modulation of bladder contractility by reducing the sensitivity of the bladder to electrical stimulation; decrease production of leukotriens and other 5-lipoxygenase metabolites	[52-58]
Epilobium parviflorum (sp. herb)	Dry extract	phenolic acids (e.g., gallic acid, chlorogenic acid, (Z)-p-coumaric acids), tannins,	Anti-inflammatory effect; inhibitionon NF-KB; inhibit hormone-dependent prostate cancer cells-(LNCaP) proliferation and PSA secretion	[59-63]

		flavonoids (e.g., myricetin, catechin, koempherol), steroids and terpenes		
Calendula officinalis	CO2 lipophillic extract, oil extract	Terpenoids, terpenes, carotenoids, flavonoids and polyunsaturated fatty acids, taraxasterol, faradiol monoester	Inhibition of the elevated levels of pro-inflammatorycytokines IL-1beta, IL-6, TNF-alpha, and IFN-gamma, aswell as the acute phase protein C-reactive protein (CRP); inhibition of LPS-induced cyclooxyge-nase-2(Cox-2) levels	[59, 63-65]
Curcuma longa	Dry extract	Curcumin	Modulation of multiple cell signaling molecules such as pro-inflammatory cytokines (tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6), apoptotic proteins, NF-κB, cyclooxygenase (COX)-2, STAT3, IKKβ, endothelin-1, malondialdehyde (MDA)	[42, 63]
Urtica dioica	Dry extract	Isolectin	Restriction or postponing of the dispersion of cells, especially malignant cells, into surrounding tissues; inhibition of the binding of androgens to their transporter proteins SHBG (Sex Hormone Binding Globulin), binding to the prostate's membrane receptors; inhibition the prostate cell membrane's enzymatic activity; immunomodulatory effects on T lymphocytes; direct inhibition cell proliferation and block of binding of epidermal growth factor to its receptor on a tumor cell line	[42, 66-70]
Melissa officinalis	Dry extract	Triterpenes (ursolic acid and oleanolic acid), phenolic acids (rosmarinic acid, caffeic acid and chlorogenic acid), and flavonoids (quercetin, rhamnocitrin, and luteolin)	Inhibition of calcium penetration into muscle cells, with a consequent reduction in the contraction of smooth muscles relief of mild symptoms of mental stress; antifungal; protective effects on sperm motility and quality of spermatogenesis	[71-75]
Malva sylvestris	Dry extract	Anthocyanins flavonoids, mucilages, terpenoids, phenol derivatives, coumarins, sterols, tannins, saponins	Anti-inflammatory, antioxidant, antitumor, antiulcerogenic and tissue integrity properties; laxative	[77, 78]
Sedum acre	Dry extract	Alkaloids	Inhibition of the adenoma and inflammation of the prostate gland, prevention and limitation of the inflammatory process,	[79, 80]

			restrains the development of hypertrophy of the glandular tissue; promotion of an increase in urine output, reduces the amount of residual urine	
Chamaenerion angustifolium (Epilobium augustifolium)	Dry extract	Oenothein B, polyphenols (gallic acid), flavonoids (quercetin derivatives), sterol	Anti-inflammatory, antitumor activity, antiproliferative, immunomodulatory, antioxidant, and antimicrobial	[81, 82]
Viscum album	Dry extract	Lectins and viscotoxins, polysaccharides, alkaloids, lipids, triterpenes	Antitumor activity, capable of stopping tumor growth, suppressing the proliferation of cancer cells, lowers blood pressure, improves heart function, and relieves vascular spasms	[83-85]
Hamamelis japonica	Dry extract	Tannins	Calm mucous membrane; astringent and hemostatic properties	[86-89]

Also, Prostant suppository (Qian Lie An Suppository) from Chinese medicine propose rich composition of ingredients that include cortex *Phellodendri*, roots of *Polygoni cuspidati*, fruits of *Gardeniae*, *Rhei* roots, and a lot of other herbals. These suppositories are recognised as safe and effective for the treatment of CP associated with damp-heat and blood-stasis syndromes [90-92]. But it is difficult to conclude the exact mechanisms of action on prostatitis and main bioactive compounds. The main component is *Phellodendron chinense* rich on alkaloid berberine and its derivatives, limonoids (obacunone), phenolic acid, quinic acid derivatives, lignans, and flavonoids responsible for anti-inflammatory effect, antibacterial effect, antiviral effect, antitumor effect, antigout effect, antiulcer effect, neuroprotective effect.

Among all plant sources, the saw palmetto appears to be the most promising for use. But its properties should be supplemented to strengthen the effect on prostatitis and complementarity of the effect.

2.1. Justification for the Use of Saw Palmetto CO_2 Extract in Suppository Development for Prostatitis Treatment

The extract of saw palmetto (*Serenoa repens*) is a widely recognized herbal supplement traditionally used in alternative medicine to alleviate urinary symptoms associated with an enlarged prostate, specifically benign prostatic hyperplasia (BPH). Its therapeutic potential and safety profile have been highlighted by several small-scale studies, which suggest its efficacy in relieving BPH symptoms [93-96].

The theoretical basis for selecting Saw Palmetto as a key ingredient in a synergistic herbal suppository formulation for prostatitis is grounded in its well-documented anti-inflammatory and anti-androgenic properties, which are central to its therapeutic effects.

Inflammation plays a significant role in the pathophysiology of prostatitis, contributing to symptoms such as pelvic pain, urinary difficulties, and discomfort. Saw Palmetto is known to possess potent anti-inflammatory properties, which are primarily attributed to its high content of fatty acids and phytosterols.

The CO_2 extract of saw palmetto fruits is a dry lipophilic extract obtained through a proprietary supercritical CO_2 extraction method [97], that retains high concentrations of essential fatty acids (oleic acid, lauric acid, and caprylic acid) and polyphenols with antioxidant properties. The raw material containing a minimum of 11% total fatty acids in the dried material [98, 99]. The biological activity and component composition of the saw palmetto extract depend on the fruit's maturity and the extraction method [100]. The primary active

groups in the CO_2 extract include fatty acids, sterols, and fatty alcohols.

Notably, variations in the extract's composition are well-documented. For example, free acid content ranges from 41% to 81% of the total lipid content, while glycerides vary between 7% and 52% [101].

These compounds can modulate inflammatory pathways by inhibiting the production of pro-inflammatory cytokines and reducing the activity of cyclooxygenase enzymes (COX-1 and COX-2), which are key mediators of the inflammatory response [102, 103].

Saw palmetto extract offers significant benefits, including not only anti-inflammatory and antiproliferative effects, but also specific inhibition of 5α-reductase enzymes. These enzymes convert testosterone to 5α-dihydrotestosterone, a potent androgen linked to BPH and potentially prostate cancer, though conclusive evidence is still pending [103,104]. The CO_2 extract demonstrates high inhibitory activity at low enzyme concentrations in prostate gland tissue, comparable to finasteride, without affecting prostate-specific antigen (PSA) secretion [105, 106]. The anti-androgenic action of Saw Palmetto is particularly beneficial in managing chronic forms of prostatitis, where hormonal imbalances may contribute to persistent symptoms.

The detailed monograph in the European Pharmacopoeia (*Ph. Eur.* 10.0) [107] on saw palmetto extract and fruit underscores its credibility as an herbal ingredient. For developing a new rectal suppository formulation, saw palmetto CO_2 extract was sourced from fruits harvested at the optimal maturity point in Florida and South Georgia, USA, in accordance with Florida Department of Agriculture and Consumer Services (FDACS) regulations. The fruits are dried within 48 hours to prevent degradation of active ingredients. The supercritical extraction method produces a lipidic sterolic extract with a composition of 85-95% fatty acids, > 23% lauric acid, 0.2-0.4% total sterols, 0.15-0.35% long-chain alcohols, and an acid value of 150-220, aligning with European Pharmacopoeia standards.

This specific extraction process and composition ensure that the saw palmetto CO_2 extract is an ideal choice for the development of suppositories aimed at treating prostatitis, leveraging its anti-inflammatory properties and enzyme inhibition capabilities for effective symptom relief.

The selection of saw palmetto for a synergistic herbal suppository formulation is based on its dual anti-inflammatory and anti-androgenic mechanisms, as well as its established role in traditional and modern therapeutic practices for prostate health. These properties make Saw Palmetto a critical component in a formulation aimed at addressing the complex pathophysiology of prostatitis, offering a targeted and potentially more effective alternative to conventional treatments.

Clinical studies have indicated that daily doses of saw palmetto extract ranging from 160 mg to 320 mg are effective [95]. Therefore, the 150 mg dosage in each suppository is within a therapeutically relevant range, ensuring sufficient bioavailability to exert its intended effect on reducing inflammation and promoting urinary health.

2.2. Justification for the Use of Lovage CO_2 Extract in Suppository Development for Prostatitis Treatment

The CO_2 extract of lovage (*Levisticum officinale*) roots is a dry lipophilic extract obtained through a proprietary supercritical CO_2 extraction method [108] is included in the theoretical formulation for a synergistic herbal suppository for prostatitis due to its notable anti-inflammatory and diuretic properties. This extraction method ensures a high-quality extract, rich in essential oils and bioactive compounds [109]. The primary components of the extract include 40-50% essential oil, with *cis*-ligustilide (45-75%) as the main constituent [110]. Other significant components include *trans*-ligustilide (3.95%), butyl phthalide, butylidene phthalides (3n-butylidene phthalide E (1.75%), 3n-butylidene phthalide Z (0.73%)), falcarinol, falcarindiol, and trace amounts of

angelicin and bergapten, β-phellandrene (0.28%), and α-terpinyl acetate (0.08%) [110, 111]. Additionally, the extract contains palmitic acid (2.81%), phytol (2.62%), linoleic acid (3.52%), stigmasterol (11%), and β-sitosterol (1.28%) [11].

Lovage root has traditionally been used in "irrigation therapy" for the treatment of pain and swelling (inflammation) of the lower urinary tract [112], for the prevention of kidney stones and to increase urine flow in cases of urinary tract infections or fluid retention. These therapeutic uses highlight its potential benefits for conditions affecting the lower urinary tract, making it a suitable candidate for inclusion in a suppository formulation aimed at treating prostatitis.

The diuretic action of lovage complements the anti-inflammatory and antimicrobial effects of saw palmetto and calendula extracts, providing an additional mechanism to support urinary health and function.

The root of *Levisticum officinale* is documented in a monograph in *Ph. Eur.* 10.0: Lovage root.

The inclusion of lovage root CO_2 extract in a suppository formulation for prostatitis treatment is justified based on several key factors: its anti-inflammatory properties (particularly, ligustilides), analgesic effects, antispasmodic activity (phthalides, such as butylidene phthalide), antioxidant properties (polyphenols and other antioxidant compounds) and diuretic effect. The presence of phytosterols such as stigmasterol and β-sitosterol contributes to the extract's ability to modulate inflammation and provide additional therapeutic benefits.

These attributes of the lovage root CO_2 extract make it a valuable addition to suppository formulations intended for the treatment of prostatitis, leveraging its multifaceted pharmacological properties to address the condition's symptoms and underlying causes effectively.

Traditionally used in herbal medicine to alleviate symptoms of urinary tract infections and to support kidney health, a 50 mg dosage of CO_2-extract ensures an effective concentration of its bioactive compounds, such as phthalides and coumarins. This dosage is formulated to provide optimal therapeutic benefits while minimizing potential adverse effects.

2.3. Justification for the Use of Calendula CO_2 Extract in Suppository Development for Prostatitis Treatment

Incorporating calendula (*Calendula officinalis*) CO_2 extract into suppository formulations offers significant therapeutic benefits for treating prostatitis, particularly through its detoxification and anti-infective properties. Calendula is renowned for its diverse bioactive constituents, which include carotenoids, flavonoids, saponins, sterols, phenolic acids, and lipids, making it an invaluable herbal ingredient for this purpose addressing the multifaceted pathology of prostatitis.

Calendula officinalis possesses a rich chemical profile. Carotenoids found in the petals and pollen, including flavoxanthin and auroxanthin, are antioxidants responsible for the plant's yellow-orange coloration [113]. Triterpenoid esters including faradiol esters, are esterified with myristic and palmitic acids, and are known for their anti-inflammatory properties [114]. Flavonoids and saponins present in the flowers and contributing to the plant’s overall therapeutic effects. Sterols are essential for modulating inflammatory responses. Phenolic acids and lipids add to the plant's anti-inflammatory and antioxidant activities [115].

The calendula flower CO_2 extract specifically contains pentacyclic triterpene alcohols, triterpenediol monoesters (including 17-28% faradiol esters), sterols, less than 0.1% carotenoids, and cuticular waxes [116]. This particular extract is recognized for its antimicrobial and anti-inflammatory properties, making it a suitable candidate for treating conditions like prostatitis, which involve both infection and inflammation.

The faradiol esters present in significant amounts within the CO_2 extract are primarily responsible for calendula’s strong anti-inflammatory effects [117]. This is crucial for managing the inflammation associated with

prostatitis, providing relief from pain and swelling.

Calendula has well-documented antimicrobial properties, making it effective against infections, including those of the urinary tract, which can exacerbate prostatitis symptoms [118]. This antimicrobial property is largely due to the presence of essential oils, flavonoids, and carotenoids in the plant, which can disrupt microbial cell membranes and inhibit their growth.

The presence of carotenoids such as lutein, zeaxanthin, and beta-carotene contribute to the antioxidant capacity of the extract, protecting prostate tissue from oxidative stress and damage.

While traditionally used for external applications like treating minor skin inflammations and wounds, the same properties that promote healing and reduce inflammation can be beneficial internally for prostate health. Its ability to stimulate collagen production and enhance tissue granulation further aids in the repair of damaged tissues. This wound-healing capability is particularly beneficial in chronic prostatitis, where persistent inflammation can lead to ongoing tissue damage.

The sterols in calendula extract aid in modulating inflammation and supporting overall prostate health.

The inclusion of calendula in the proposed suppository formulation not only complements the actions of other herbal ingredients but also enhances the overall efficacy of the formulation in managing this challenging condition.

The flowers of *Calendula officinalis* are subject to a monograph in the *Ph. Eur.* 10.0: Calendula flower. This ensures that the extract meets rigorous standards for quality and efficacy. Suppliers in Central Europe produce Calendula flowers with a high content of faradiol esters, ensuring the extract's potency and consistency [119].

The 50 mg dosage of CO_2-extract in each suppository is designed to enhance local anti-inflammatory effects, promote healing of the mucosal tissue, and provide relief from discomfort associated with urinary conditions.

The supplier of lovage roots and marigold flower CO_2-extracts source herbal raw materials from all continents.

All botanical raw material is subjected to strict selection and examination in accordance with GACP (Good Agricultural and Collection Practices) guidelines [120].

The combination of these extracts is intended to produce a synergistic effect, where the collective action of saw palmetto, lovage, and calendula extracts enhances the overall therapeutic efficacy. This multi-targeted approach aims to provide comprehensive relief from symptoms associated with BPH, urinary tract infections, and inflammation.

III. FORMULATION DESIGN AND THEORETICAL CONSIDERATIONS

The use of a suppository as the delivery system for herbal extracts in the treatment of prostatitis offers several theoretical advantages, particularly in terms of improved bioavailability and localized action.

Suppositories deliver active ingredients directly to the rectal or vaginal mucosa, where they are rapidly absorbed into the bloodstream. This bypasses the digestive system and first-pass metabolism in the liver, which can otherwise degrade or alter the active compounds [121]. Consequently, this route can enhance the bioavailability of the herbal extracts compared to oral administration, where significant amounts of the active ingredients might be metabolized before reaching systemic circulation. This localized approach helps minimize potential adverse effects on other organs and systems.

Although the CO_2 extracts are obtained without the involvement of toxic organic solvents, the biologically active substances themselves can cause a certain range of side effects [122, 123]. This localized approach helps minimize potential adverse effects on other organs and systems, focusing treatment where it is needed most.

The suppository formulation allows for a higher concentration of active ingredients at the site of absorption [124]. This can lead to more effective and targeted delivery of the herbal extracts to the prostate area, which is crucial for

managing localized conditions such as prostatitis.

Suppositories protect the herbal extracts from the harsh conditions of the gastrointestinal tract, such as acidic pH and digestive enzymes, which can degrade sensitive compounds.

When combined with saw palmetto and calendula, lovage's anti-inflammatory effects can enhance the overall efficacy of the formulation. Each herb targets different aspects of the inflammatory process, leading to a more robust reduction in inflammation and associated symptoms.

The diuretic properties of lovage extract support urinary health, which is crucial for managing prostatitis. By promoting urine flow and reducing urinary retention, it complements the effects of saw palmetto, which helps modulate hormonal influences on the prostate, and calendula, which aids in tissue healing and inflammation control.

The combined action of anti-inflammatory and diuretic effects from lovage, along with the synergistic properties of saw palmetto and calendula, can lead to a more comprehensive approach to treating prostatitis. This multi-faceted strategy addresses inflammation, infection, and urinary issues simultaneously, potentially improving patient outcomes and quality of life.

The theoretical synergy arises from the integrated mechanisms of each herb. Together, they address multiple facets of prostatitis—namely inflammation, infection, and urinary issues.

The suppository form ensures direct delivery of these herbal extracts to the affected area, which can enhance the absorption and effectiveness of the active compounds. The combined therapeutic actions of the herbs can lead to improved bioavailability and targeted action.

Therefore, based on the proposed synergistic interactions and the known effects of saw palmetto, calendula, and lovage, the following potential therapeutic outcomes can be hypothesized for the herbal suppository formulation in treating prostatitis: enhanced reduction in inflammation, improved symptom relief and quality of life, better management of chronic prostatitis, enhanced healing and tissue repair, effective infection control, improved urinary function and comfort, and reduced systemic side effects.

IV. CONCLUSION

The formulation's synergistic effects on reducing inflammation, modulating the immune response, and controlling infections could offer superior therapeutic outcomes compared to 5α-reductase inhibitors existing treatments [105-106]. This may lead to more effective symptom management, reduced reliance on conventional medications, and improved patient satisfaction.

The suppository form allows for targeted delivery of herbal extracts directly to the affected area, potentially providing more effective and rapid relief from localized symptoms of prostatitis. This localized action might result in quicker symptom resolution and fewer systemic side effects.

Compared to oral medications such as α-blockers, NSAIDs (Nonsteroidal Anti-Inflammatory Drugs), fluoroquinolones or sulfamethoxazole-trimethoprim [105-106], the suppository formulation might reduce the risk of systemic side effects, such as gastrointestinal discomfort or liver strain, which are common with many conventional treatments. This could make the treatment more tolerable for patients.

The formulation could offer a complementary or alternative option for patients who do not respond well to conventional treatments or who experience adverse effects from existing medications.

If proven effective, the suppository could be used as a primary treatment option for prostatitis, especially in cases where inflammation, infection, or urinary symptoms are prominent. Its holistic approach could offer a comprehensive solution addressing multiple aspects of the condition.

The formulation could be used alongside conventional treatments to enhance overall efficacy. For instance, it could complement antibiotic or anti-inflammatory therapies by providing additional benefits such as improved tissue repair and infection control.

Given its herbal composition, such a suppository formulation could be tailored to

individual patient needs based on their specific symptoms and treatment responses. This personalization could enhance treatment outcomes and patient compliance.

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СИНЕРГІЯ РОСЛИННИХ СКЛАДНИКІВ В СУПОЗИТОРІЯХ ДЛЯ ЛІКУВАННЯ ПРОСТАТИТУ

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Проблематика. Поширеність захворювань передміхурової залози, включно із простатитом, становить за світовими даними від 11% до 74% у віці 20-65 років. Існують чіткі стандарти як консервативного, так і хірургічного лікування захворювань передміхурової залози. Однак консервативне медикаментозне лікування простатиту не завжди дозволяє приймати препарати протягом тривалого періоду (6-8 тижнів) через можливі побічні ефекти. Наразі існує потреба у продуктах, які б вирізнялися високою ефективністю при максимальній безпеці, що могло б забезпечити їх тривале і безболісне застосування. На цьому фоні особливий інтерес становлять нові багатокомпонентні фітопродукти, які активно впливають на функціональний стан передміхурової залози.
Мета. Теоретичне дослідження синергетичної композиції трав'яних супозиторіїв для лікування простатиту з використанням CO_2-екстрактів *Serenoa repens, Calendula officinalis* і *Levisticum officinale*.
Методика реалізації. Вивчено та проведено аналіз наукових досліджень науковців різних країн, а також міжнародно визнаних монографій щодо фітоінгредієнтів, які відомі своїми терапевтичними властивостями при лікуванні простатиту. Проаналізовано дані з наукових джерел щодо можливої комбінації та досягнення позитивної синергії для CO2-екстрактів любистку лікарського (*Levisticum officinale*), карликової пальми (*Serenoa repens*) та календули лікарської (*Calendula officinalis*).
Результати. Кожен трав'яний екстракт був обраний на основі його унікальних терапевтичних властивостей і потенціалу доповнювати один одного. Карликова пальма (*Serenoa repens*) має протизапальну та антиандрогенну дію, спрямовану на запалення та збільшення простати. Календула лікарська (*Calendula officinalis*) має протизапальну, протимікробну та ранозагоювальну дію, сприяючи зменшенню запалення та відновленню тканин. Любисток (*Levisticum officinale*) має протизапальні та сечогінні властивості, допомагаючи зменшити запалення та покращити функцію сечовипускання.
Висновки. Очікується, що теоретична синергія досліджуваних екстрактів підвищить загальну терапевтичну ефективність, пропонуючи покращене полегшення симптомів, контроль інфекції та регенерацію тканин порівняно з традиційними методами лікування. Очікується, що система доставки супозиторіїв забезпечить локалізовану дію зі зниженими системними побічними ефектами. Запропонована формула має потенціал як додаткове або альтернативне лікування простатиту, очікуючи на подальшу експериментальну перевірку та клінічні випробування.

Ключові слова: простатит, протектор передміхурової залози, рослинні інгредієнти, карликова пальма, календула лікарська, любисток лікарський, синергетична композиція, клінічна оцінка.