# CHAPTER 2

# LITERATURE REVIEW

# REVIEW OF LITERATURE

**Jagtap PN et al (2023)** The study selected potent antiurolithiatic herbs to assess the efficacy of a polyherbal tablet. This tablet consisted of Tribulus terrestris, Musa balbisiana colla, Bryophyllum pinnata, and Commiphora wightii. The antiurolithiatic activity of the tablets was tested using Wistar rats to combat renal calculi induced by ethylene glycol.[106]

**Alomair MK et al (2023)** investigated the potential anti-urolithic properties of grape seed extract (GSE) using a rat model of experimental urolithiasis induced by ethylene glycol (EG) and ammonium chloride (AC). Their findings indicate that GSE demonstrated protective effects against EG-induced renal stones, as shown by improvements in kidney function, reduction in histological damage, and decreased formation of oxalate crystals. These effects are likely attributed to the antioxidant and anti-inflammatory properties exhibited by the extracts.[107]

**Golla S et al (2023)** The current study assessed the potential anti-urolithic effects of Cyperus rotundus tubers extract using in silico, in vitro, and in vivo approaches. In silico analysis focused on the constituents of Cyperus rotundus and the pathological protein oxalate oxidase (PDB Id: 2ETE). In vivo experiments examined the effects of the ethanolic extract (administered at doses of 100, 200, and 400 mg/kg body weight) on rats induced with sodium oxalate urolithiasis for seven days. The results demonstrated that the ethanolic extract of Cyperus rotundus tuber prevented sodium oxalate-induced stone formation, corroborated by molecular docking studies.[108]

**Kishor P et al (2022)** carried out preparation and standardization of polyherbal extract of *T. terrestris* L., *Avera lanata* L., *Crataeva religiosa* hook. And *Emblica officinalis* L. I suspension base showed good stability and redispersibility. Male mice chosen, existing research show that having the property like stone discharge through female mice had been substantially lower.[109]

**Sharma YK et al (2022)** *Citrus limon L., Citrus aurantium L., and Citrus medica L.* are known for their medicinal properties, including antiurolithic activity, treatment of stomach ache, vomiting, as well as their antifungal and antibacterial effects. In a study, urolithiasis was induced in rats using ethylene glycol. The combined extract of all three plants at a dose of 300 mg/kg showed significant efficacy compared to when each plant was administered

individually. The analysis included measurement of calcium, phosphate, magnesium, creatinine, uric acid, protein, urea nitrogen, and oxalate levels.[110]

**Kamaraj MC et al (2022)** The DPPH free radical scavenging assay was employed to assess free radical scavenging activity. Rutin served as a positive control. An acute toxicity study was carried out using Wister albino rats, which indicated no adverse effects on liver and renal functions fifteen days post-administration. These findings provide scientific support for considering the polyherbal formulation as a promising treatment for chronic kidney disease.[111]

**Wanjari MM et al (2022)** In both acute and sub-acute toxicity studies, administration of gokshuradiguggulu showed no significant changes in parameters or adverse effects compared to the control group treated with the vehicle. No instances of mortality or moribund states were observed across any groups in either study. The administration of gokshuradiguggulu at both acute and repeated doses over 28 days did not demonstrate any toxicity or adverse effects at the administered doses, with a determined No Observed Adverse Effect Level (NOAEL) of 2700 mg/kg.[112]

**Venkatesan H et al (2022)** In this study, we evaluated the antiurolithiatic effects of Aavarai Bhavanai Chooranam (ABC) in Wister albino rats with ethylene glycol-induced urolithiasis. We analyzed urine levels of calcium, magnesium, oxalate, inorganic phosphate, protein, and creatinine. ABC treatment was found to increase urine output and maintain alkalinity in the urinary tract, which likely contributes to its antilithiatic properties. Furthermore, ABC demonstrated protective effects on kidney structure and function, enhancing physiological mechanisms that deter stone formation. These findings support the clinical efficacy of ABC in kidney health maintenance.[113]

**Ogoun T R et al (2022)** The study aimed to examine the impact of Yoyo cleanser bitters, a popular Nigerian polyherbal preparation, on the biochemical functions of the liver and kidney in albino rats. The findings suggest that the polyherbal formulation, administered at the specified doses and duration, did not induce cholestasis or impair the liver's ability to excrete bilirubin, as indicated by levels of AST, ALP, albumin, total bilirubin, and protein. Furthermore, the formulation did not appear to have nephrotoxic effects on the kidneys, as evidenced by the decreased levels of creatinine observed in the study.[114]

**Mishra A et al (2022)** WHO has identified Urolithiasis, also known as urinary calculi or stones, as a prevalent urinary tract condition globally. It involves the formation of calcifications within the urinary system. Urolithiasis poses a significant worldwide health concern. Several therapeutic agents, such as NSAIDs, aminoglycoside antibiotics, and chemotherapeutic agents, have been incorporated into medical treatments in recent years. However, these medications carry risks of adverse effects on the kidneys, potentially leading to acute renal failure, chronic interstitial nephritis, and nephrotic syndrome. [115]

**Jagtap PN et al, (2021)** The polyherbal formulation, Lithout tablets, was prepared using the Wet Granulation method. The study findings indicate that animals administered with the standard drug (Cystone) and Lithout tablets at a dosage of 200 mg/kg showed considerable anti-urolithiatic activity. Furthermore, they exhibited protection against tubular interstitial damage in both kidneys and liver in ethylene glycol-induced urolithiatic rats. [116]

**Khan A et al, (2021)** Conducted a comprehensive literature review on the efficacy of different herbal treatments in rat models of calcium oxalate (CaOx) urolithiasis. Favorable outcomes such as decreased stone size, reduced number of stones, and facilitated passage were evaluated.[117]

**Swati Sharma et al, (2021)** The prepared Trikantakadikvatha churn tablets demonstrate crystal inhibition over time, with the extent of inhibition varying with drug concentration. At a concentration of 1000 µg/ml, the tablets achieved a maximum crystal inhibition of 76.25%. Furthermore, the developed dosage forms of Trikantakadikvatha ghan vati (TKGV) are more stable than the decoction (kvatha) and show promising results in the treatment of Urolithiasis (Mutrakrichra).[118]

**Sachin M. Mahajan et al, (2021)** The polyherbal suspension was formulated using alcoholic extracts of Curcuma caesia, Citrullus lanatus, Evolvulus alsinoides, Gymnema sylvestre, Tinospora cordifolia, Caesalpinia bonduc, and Withania coagulans. The resulting Polyherbal Formulation-C exhibited a pleasant appearance and texture. No changes were observed in sedimentation, flow rate, pH, viscosity, or other physicochemical parameters. This suspension, composed of ethanolic extracts, appears to be effective and safe for use in combinational therapy.[119]

**Supriya S. Chimagave et al, (2020)** The antiarthritic activity of the polyherbal formulation against Freund's complete adjuvant-induced paw edema demonstrates significant effects at

all three doses (250, 500, and 750 mg/kg p.o), markedly reducing paw swelling. This formulation provides a substantial protective effect against paw edema induced by Freund's complete adjuvant in rats.[120]

**Harikesh Maurya et al, (2019)** A polyherbal dispersible tablet formulated with A. officinal, *B. diffusa*, C. papaya, C. fistula, C. intybus, F. hispida, F. indica, C. nurvala, S. virgaurea, and V. negundo was developed for managing kidney disorders. The PHF-3 formulation demonstrated satisfactory disintegration and in vitro dispersion time, attributed to the inclusion of cross povidone, and was identified as the best formulation. Stability studies and IR compatibility tests confirmed that PHF-3 could represent a new, easily swallowable dispersible tablet, potentially enhancing drug permeability and improving bioavailability for nephrotic patients.[121]

**Patel N et al, (2019)** To evaluate the acute oral toxicity of the Uricare Tablet, an anti- BPH herbo-mineral formulation, on Swiss albino mice and its efficacy against Benign Prostatic Hyperplasia (BPH), a study was conducted. No mortality was observed in any group. The Uricare Tablet demonstrated significant effects on body weight, urine volume, and various prostatic and biochemical parameters. The results indicate that the Uricare Tablet does not produce any toxic effects at a dose of 2000 mg/kg, and the normal values of kidney markers and physical prostate parameters suggest its effectiveness against BPH.[122]

**Baheti D et al, (2013)** A studied increase in biochemical parameters such as ACP, ALP, AST, and ALT levels, along with a decrease in LDH levels in the kidney homogenate, indicated the induction of urolithiasis. Daily oral treatment with a polyherbal formulation indicated the induction of urolithiasis. Daily oral treatment with a polyherbal formulation (PHF) consisting of Plectranthus mollis Spreng, Didymocarpus pedicellata, Teraxacum officinale, Dendrophthoe elastic Desr, and Citrus medica at doses of 300 and 400 mg/kg not only significantly decreased the quantity of calcium oxalate deposited in the kidneys but also reversed all the biochemical changes induced by calcium oxalate urolithiasis, thereby supporting its traditional use.[123]

**Gilhotra UK et al, (2013)** Hydroalcoholic extracts of Kalanchoe pinnata and Rotula aquatica, as well as their combination, were formulated into herbal tablets and evaluated for their antilithiatic properties using an in vitro method. The homogeneous precipitation

method was employed, and the study was conducted in glass tubes using TRIS buffer at pH 7.4. The herbal tablet formulation containing Kalanchoe pinnata and Rotula aquatica demonstrated an inhibitory effect on calcium oxalate crystallization, indicating potential benefits in the treatment of renal lithiasis.[124]

**Bodakhe KS et al, (2013)** The study investigated the protective effects of Cystone on oxidative stress and calcium oxalate crystal formation in hyperoxaluria-induced urolithiasis. In untreated animals, EG treatment resulted in a higher urine volume, lower urinary pH, and increased urinary excretion of oxalate, calcium, and phosphate. Cystone treatment demonstrated a protective role by enhancing renal antioxidant status and promoting diuresis, thereby mitigating oxidative stress and calcium oxalate crystal deposition. [125]

**Deng G et al (2011)** Xiao-Chai-Hu-Tang, also known as Sho-sai-ko-to (SST), is a traditional East Asian herbal formulation comprised of seven botanical extracts commonly used to treat liver diseases. Studies have indicated that SST can lower transaminase levels and decrease the incidence of hepatocellular carcinoma in patients with hepatitis B. To explore its potential benefits for hepatitis C patients ineligible for interferon-based treatments, we performed a phase II clinical trial to assess whether SST merits additional investigation.[126]

**M. G. Shekar Kumaran, et al (2011)** The Ayurvedic formulation studied led to a notable reduction in the size of renal calculi, unlike the placebo group where no size reduction was observed. Patients receiving the Ayurvedic treatment showed improvements in clinical symptoms such as hematuria, frequent urination, and tenderness in the kidney, ureter, and bladder (KUB) area. Additionally, there was a significant decrease in the number of urinary red and white blood cells and serum uric acid levels in these patients. This formulation appears to be safe and effective for individuals with smaller kidney stones, enhancing the rate of stone expulsion. [127]

**Jain PK et al, (2010)** A novel, straightforward, sensitive, precise, and reliable highperformance thin layer chromatographic (HPTLC) method has been developed for estimating andrographolide in herbal extracts and pharmaceutical formulations. The method resulted in compact spots for andrographolide, with an Rf value of 0.49. Calibration plot data indicated a strong linear relationship, with an $r^2$ value of 0.9986 within the

concentration range of 200 ng to 1000 ng based on peak area. The detection and quantification limits were established at 3.5 ng and 11.7 ng, respectively.[128]

**Mohamme D. et al (2010)** This study involves formulating a gel using Pothos scandens Linn (P. scandens) leaf extract and evaluating its effectiveness in healing burn wounds. The dried leaves of P. scandens were extracted with ethanol and underwent preliminary phytochemical evaluation as well as wound healing activity studies. Various gel formulations containing 4% (w/v) ethanolic extract of P. scandens were prepared with polymers carbopol 934 and carbopol 940 at different concentrations.[129]

**Das et al (2010)** The formulation containing 2.5% Stevia extract demonstrated superior stability compared to other formulations and the control sample. Evaluation of various parameters indicated no toxicity or skin irritation, suggesting this Stevia extract formulation is both safe and beneficial for use.[130]

**Ajazuddin et al (2010)** This review provides an overview of the present state of novel herbal formulation development, detailing their preparation methods, active ingredient types, particle size, entrapment efficiency, administration routes, biological activities, and diverse applications.[131]

**Shirfule AL et al (2009)** A polyherbal formulation comprising *Tribulus Terrestris* L., *Ricinus communis* L. roots, *Solanum indicum* L., *Hygrophila spinosa* L. seeds, and *Solanum surattense* L. aerial parts is utilized for the management of kidney stones. The active components, identified as saponins, were analyzed using high-performance thinlayer chromatography. Patients with naturally induced urolithiasis were administered 1 g of the powder mixed with an equal volume of honey and fresh curd (1 teaspoonful) orally for 28 days. Ultrasonography performed before and after treatment indicated complete elimination of calculi or reduced stone growth in the majority of patients.[132]

**Sutar NG et al, (2009)** The antipyretic activity of an ethanolic extract from *Moringa oleifera* Lam. seeds was investigated in albino rats under normal body temperature and yeast-induced pyrexia conditions. The ethanol extract was administered orally at doses of 100, 200, and 300 mg/kg body weight. It exhibited a significant, dose-dependent reduction in both normal body temperature and yeast-induced fever. The antipyretic effect of the

ethanolic seed extract was found to be comparable to that of Paracetamol (150 mg/kg body weight, oral route), a standard antipyretic agent. [133]

**Lakshmi V et al (2009)** The antidiuretic activity of *Moringa oleifera* pods has been established. In the present study, the aqueous extract of Moringa oleifera pods was tested for diuretic activity in albino rats at two oral doses (400 mg/kg and 800 mg/kg). The diuretic effect of the extract was compared with that of the standard drug hydrochlorothiazide. The findings concluded that Moringa oleifera exhibits diuretic action.[134]

**Jaiswal D et al (2009)** The effects of *Moringa oleifera* Lam. leaves aqueous extract on hyperglycemic rats were investigated. In animals with sub and mild diabetes, the extract caused a significant decrease in glucose levels, with reductions of 31.1% and 32.8% respectively, during OGTT (Oral Glucose Tolerance Test). Moreover, there was a notable decrease in urine sugar levels from +4 to nil, and urine protein levels from +2 to trace. These findings provide scientific validation for the traditional use of M. oleifera in treating diabetes mellitus.[135]

**Hamman JH et al (2008)** The latest research has explored additional effects and uses of Aloe vera leaf gel. These include its potential to improve the absorption and availability of co-administered compounds when used in liquid preparations of whole leaf or inner fillet gel. Furthermore, Aloe vera has shown promise in enhancing skin permeation. Additionally, there are significant pharmaceutical applications, such as using dried Aloe vera gel powder as an excipient in sustained-release pharmaceutical formulations.[136]

**P.M. Dandgi et al, (2008)** Polyherbal suspensions were developed using extracts that exhibited notable activity and were assessed for their physicochemical properties and hepatoprotective effects, alongside LIV-52 as a standard reference. It was observed that the F3 formulation, comprising chloroform, petroleum ether, and aqueous extracts of Ferula asafoetida, petroleum ether and ethanol extracts of *Momordica charantia* Linn., and petroleum ether and ethanol extracts of *Nardostachys jatamansi*, displayed considerable hepatoprotective activity possibly attributed to the synergistic effects of these extracts.[137]

**Kaur A D et al (2008)** A novel, straightforward, sensitive, accurate, and sturdy high performance thin-layer chromatography (HPTLC) method was developed to quantify conessine in herbal extracts and pharmaceutical formulations. The chromatographic

separation employed a twin trough glass chamber saturated with a mobile phase comprising toluene, ethyl acetate, and diethyl amine (6.5:2.5:1, v/v/v) at room temperature (25 ± 2 °C) via linear ascending development. This system reliably produced well-defined spots for conessine with an Rf value of 0.82. Calibration plots exhibited excellent linearity with an r2 value of 0.9998 over a concentration range of 1–10 µg, as determined by peak area analysis. [138]

**Ram Kumar Roy et al, (2007)** The onset of hair growth was significantly shortened to one-third compared to control animals when treated with the formulated product. Moreover, the duration for complete hair regrowth was reduced by 32%. Analysis of the hair growth cycle following treatment with both the formulation and minoxidil (2%) revealed a higher count of hair follicles in the anagen phase compared to the control group. These findings support the well-known hair growth-promoting properties attributed to the plants traditionally. Additionally, the formulated product demonstrates promising potential for treating alopecia.[139]

**Ahemad B. et al (2006)** The methanol extract of Moringa fruit was investigated for its potential anti-inflammatory properties using a rat paw edema model induced by carrageenan. The results showed dose-dependent inhibition of edema, indicating significant potency of the extract. It contains anti-inflammatory compounds that could be beneficial for treating acute and chronic inflammatory conditions. Additionally, Moringa oleifera Lam. (Moringaceae) was studied for its analgesic effects against thermal stimuli using Eddy's hot plate test and Analgesiometer test, as well as for its antipyretic effects.[140]

**Siddiq A et al, (2005)** The antioxidant potential of *Moringa oleifera* leaves could be linked to their rich content of flavonoids, polyphenols, and tocopherols. The findings suggest that M. oleifera leaves have the potential to be utilized as a promising source of natural antioxidants and nutraceuticals.[141]

**Siddhuraju P et al (2003)** The antioxidant activities and free radical scavenging capacities of water, aqueous methanol, and aqueous ethanol extracts from freeze-dried *Moringa oleifera* Lam. leaves sourced from various agro-climatic regions were assessed. Results indicate that all leaf extracts effectively scavenged peroxyl and superoxyl radicals. This

study underscores the potential of Moringa leaves as a rich natural source of antioxidants, owing to their significant antioxidant activity.[142]

**Lalas S et al, (2002)** According to the study, aqueous, methanol (80%), and ethanol (70%) extracts of freeze-dried *Moringa oleifera* leaves demonstrated significant radical scavenging and antioxidant properties. These extracts exhibited the ability to scavenge peroxyl and superoxyl radicals. The primary bioactive compounds identified were quercetin and kaempferol. Additionally, the oil extracted from dried Moringa oleifera seeds exhibited superior antioxidant activity compared to butylated hydroxytoluene and α-tocopherol.[143]