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DEVELOPMENT AND EVALUATION OF A POLYHERBAL FORMULATION AGAINST GLOMERULONEPHRITIS, INTERSTITIAL NEPHRITIS AND POLYCYSTIC KIDNEY DISEASE

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ABSTRACT

This research focuses on the development and evaluation of a polyherbal formulation targeting Glomerulonephritis, Interstitial Nephritis, and Polycystic Kidney Disease. The formulation comprises a combination of herbs, each with potent anti-nephrotic properties. Angelica officinalis aids in urinary retention, while Boerhavia diffusa acts as an effective diuretic. Carica papaya serves as an immunomodulator and aids in kidney tissue regeneration, while Cassia Fistula protects against DNA damage. Additionally, Cichorium intybus modulates kidney function and exhibits immunomodulatory effects, and Ficus hispida inhibits insulinase activity in the liver and kidneys. Fumaria indica plays a crucial role in reducing granuloma mass, and Crataeva nurvala supports kidney health by preventing microbial infections and aiding in urinary retention. Solidago virgaurea stimulates kidney function, and Vitex negundo acts as a tonic for nephrotic disorders with diuretic properties. The current polyherbal drugs available in the market often require high doses, leading to increased workload on normal kidney function and potential side effects. This study aims to develop a novel polyherbal dispersible tablet using scientifically validated plant extracts, providing effective treatment for kidney diseases while reducing economic burden and treatment costs. Physicochemical parameters of the prepared tablets were evaluated, and the optimized formulation was found to be stable under accelerated conditions. This research offers a promising avenue for the development of cost-effective and efficient treatments for kidney diseases.

Keywords *– Glomerulonephritis, Polyherbal formulation, Carica papaya, Crataeva nurvala, Vitex negundo.*

1. INTRODUCTION

The kidneys are vital organs responsible for numerous functions, including the removal of toxins from the body [1]. They function as a complex multitasking unit within the body, regulating endocrine function, acid-base balance, blood pressure, and erythropoiesis to ensure normal bodily functions.

However, kidney function can become impaired when urinary functions decline due to various conditions, even those unrelated to kidney pathology [2]. Glomerulonephritis, characterized by inflammation and cell proliferation within the glomerulus, poses a significant concern for kidney health [3].

The nephron, the basic functional unit of the kidney, consists of a network of renal capillaries that filter plasma across the glomerular basement membrane (GBM) and podocyte slit diaphragms into Bowman's space [4]. In healthy adults, the kidneys filter over 150

Liters of plasma per day through millions of glomeruli before excreting toxins into the pelvis as urine [5]. However, this high filtering capacity exposes the capillary vessels to potential injury from immune cells and soluble products [6,7].

Glomerulonephritis encompasses various immune-mediated disorders that cause inflammation within the glomerulus and other filtering units of the kidney, often leading to end-stage renal disease (ESRD) [8]. Chronic glomerulonephritis is a significant concern globally, particularly in developing countries where the cost of treatment is often prohibitive for many patients [9,10]. For example, in India, approximately 90% of patients may not be able to afford lifelong treatment costs associated with chronic glomerulonephritis. The herbs investigated in this study exhibit potent anti-nephrotic activity and contribute to kidney health through various mechanisms. *Angelica officinalis* is known for its role in urinary retention, while *Boerhavia diffusa* acts as a powerful diuretic, promoting the elimination of excess fluids from the body. *Carica papaya* serves as an immunomodulator and aids in the regeneration of kidney tissues. *Cassia Fistula* protects against DNA damage, while *Cichorium intybus* exhibits immunomodulatory effects and helps regulate kidney function. *Ficus hispida* inhibits insulinase activity in the liver and kidneys, contributing to metabolic balance. *Fumaria indica* plays a vital role in reducing granuloma mass, while *Crataeva nurvala* supports kidney health by preventing microbial infections and aiding in urinary retention. *Solidago virgaurea* stimulates kidney function and supports overall kidney health, and *Vitex negundo* serves as an excellent tonic for nephrotic disorders, with additional diuretic properties [11].

2. MATERIALS AND METHODS

2.1 Materials

The herbs used in the study have potent anti-nephrotic activity and individually play a crucial role as follows; *Angelica officinalis* responsible for urinary retention, *Boerhavia diffusa* act as excellent diuretic, Carica papaya act as immunomodulator and recover kidney tissues*, Cassia Fistula* protects deoxyribose from damage, *Cichorium intybus* has good immunomodulatory action and modulate kidney function, *Ficus hispida* inhibits insulinase activity of liver and kidney*, Fumaria indica* play a crucial role in reduction of granuloma mass, *Crataeva nurvala* support kidney from microbial infection and act as urinary retention, *Solidago virgaurea* stimulates the kidneys with excellent support of kidney health and *Vitex negundo* is an excellent tonic for nephrotic disorder with good diuretic properties. Roots of above plants were cleaned, shade dried, and powdered by a mechanical grinder.

2.2 Extraction

The grounded root powder of each plant (500g) was separately added to the 2 Liter distilled water and stored at room temperature for 48 hours. Thereafter, extracts were separately filtered by using Whatman filter paper, concentrated at reduced temperature (40°C) on a rotary evaporator, and freeze dried to get extract powder [yield 18-20% (w/w)]. Extract powder(s) were stored in the air- tight containers. Similarly, methanolic extract of each drug was prepared. Both methanol and aqueous extracts of polyherbal combination were tested for glomerulonephritis activity in animal and as methanol extract has not shown desirable activity so that further studies were made on aqueous extract only.

2.3 Preparation of polyherbal dispersible tablet

The plants root extract obtained from methanol and aqueous solvent have been composed separately in an appropriate quantity based on lowest dose of each plant as reported for promising activity has been preferred for the preparation of the potent polyherbal combination [12] used in the treatment of glomerulonephritis.

Polyherbal dispersible tablets were prepared separately through geometrical dilution mixing and direct compression method (Punching machines, Cadmach CMS-15 No. H/513/11-12), using powdered extracts, disintegrating agents, talc and other excipients. All the ingredients were passed through mesh sieve no. 120 and then mixed each other as per geometrical dilution method to maintain uniformity. The powder mixtures possess good flow properties and good packing ability, so the mixtures were directly compressible [13,14]. Nine formulations were prepared by using all ingredients in appropriate quantity but the disintegrants was used in different concentration only and denoted by PHF-1 to PHF-9 (Table 1).

Table 1: Composition of polyherbal formulation for dispersible tablets

Ingredients (mg/tab)	PHF- 1	PHF- 2	PHF- 3	PHF- 4	PHF- 5	PHF- 6	PHF- 7	PHF- 8	PHF- 9
Aqueous Extracts Mix (Each extract 25 mg x 10 Plants = Total 250mg)	250	250	250	250	250	250	250	250	250
β-cyclodextrin	200	200	200	200	200	200	200	200	200
Crospovidone	15	20	25	--	--	--	--	--	--
Sodium Starch glycolate	--	--	--	15	20	25	--	--	--
Croscarmellose sodium	--	--	--	--	--	--	15	20	25
Microcrystalline cellulose	65	60	55	65	60	55	65	60	55
Sodium Saccharin	10	10	10	10	10	10	10	10	10
Mg. Stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Total Weight	550	550	550	550	550	550	550	550	550

2.4 Evaluation of Polyherbal Dispersible Tablet

2.4.1 Weight variation test

The weight variation of tablets was carried out to ensure that, each of the tablets contains the proper amount of drug. The test was performed by weighing 20 tablets individually using an analytical balance, then calculated average weight and compared the individual tablet weights. The percentage weight variation was calculated.

2.4.2 Hardness test

The hardness of the tablet is defined as the loads required for crushing or fracture a tablet by placing on its edge. The confrontation of tablets for capping, abrasion or breakage under storage conditions, transportation and handling before usage depend on tablet hardness (kg/cm^2). The hardness test was performed by using Monsanto hardness tester (Harrison's). The instrument measures the force required to break the tablet when the force (Kilogram-force) generated by anvils to the tablet. The tablet was placed between two anvils; the force applied to the anvils and the crushing strength that causes the tablet to break was recorded and the crushing strength test was performed on 20 tablets of each formulation.

2.4.3 Friability test

The friability test was performed by using tablet friability tester (Veego). Ten tablets of each formulation were weighed and tested at a speed of 25 rpm for 4 min (100 rotations). After removing of dust, tablets were re-weighed and friability percentage was calculated.

2.4.4 Drug content uniformity test

From each formulation, 20 tablets were taken, weighed and thoroughly triturated. The sufficient amount of the powder equivalent to 250mg of the drug was accurately weighed and diluted in 300ml of 0.1N HCl for 10min with vigorous shaking. Further, this prepared mixture was diluted with 0.1N HCl up to 400ml and then filtered. 10ml of this filtrate diluted in 100ml distilled water and the absorbance was taken at the wavelength of λmax 200-400nm by using double beam UV spectrophotometer [15,16].

2.4.5 Disintegration time

From each formulation 6 polyherbal dispersible tablets were randomly selected to determine the disintegration time. The acidic buffer (pH 1.2) was used as a disintegration medium and temperature was maintained at 37±0.5°C. The average disintegration time of six tablets was taken [17].

2.4.6 Dispersion time

In-vitro dispersion time of polyherbal dispersible tablet was measured by dropping the tablet in a beaker containing 100ml of normal water. Two tablets from each formulation were randomly selected and in-vitro dispersion time was determined. A smooth dispersion is produced, which passes through a sieve screen with a nominal mesh aperture of 710µm [18].

2.4.7 In-vitro dissolution study

In the regulations for dissolution testing of herbal medicines particularly difficult to oversee authority requirements for dissolution testing of herbal medicines due to widely varying regulations. Since the phytoconstituents of medicinal plant and other ingredients of the polyherbal combination covers the multiple constituents, so that the development of dissolution method becomes more complex than for defined single constituent. Hence the in-vitro dissolution test was not performed for polyherbal dispersible tablet [19].

2.4.8 Accelerated stability study

Stability study was carried out as per ICH guidelines for polyherbal combination to check the physical, chemical and physiological property of prepared formulation in a short period of time. The optimized polyherbal formulation was subjected to accelerated stability studies and the formulations were packed in bottles at specified conditions of temperature and relative humidity i.e., 25°C/60% RH, 30°C/65% RH and 40°C/75% RH for 3 months [20].

3. RESULTS AND DISCUSSION

3.1 Formulation and characterization of tablet

Nine formulations were prepared for polyherbal dispersible tablets having each of 550 mg weight compressed by 10-station Mini Press-I rotary tablet compression machine fitted with 12mm punches size. None tablet manufacturing defects like capping, lamination and chipping were observed. The prepared dispersible tablets were subjected for evaluation of characteristic parameters like size, shape, color, and appearance.

The dispersible tablets were non-sticky and appeared as good-quality. The diameter and thickness of each tablet were performed with 20 tablets by using digital Vernier scale during the physical study because it permits accurate measurements and provides information about variations between tablets of formulations (Table 2).

Table 2: Physical description of polyherbal dispersible tablets

S. No.	Parameter	Result
1.	Color	Yellowish-Brown
2.	Shape	Round, Biconvex
3.	Odor	Characteristic odor
4.	Taste	Pleasant taste
5.	**Size in mm**	
	i. Thickness	5.12±0.08 mm
	ii. Diameter	12.17±0.01 mm

The average thickness of tablet was found to be 5.12±0.08mm with average diameter of 12.17±0.01mm found during the evaluation and development of tablets (Table 2). Organoleptic properties of prepared polyherbal dispersible tablet show yellowish- Brown colour and almost round in shape (Figure 1).

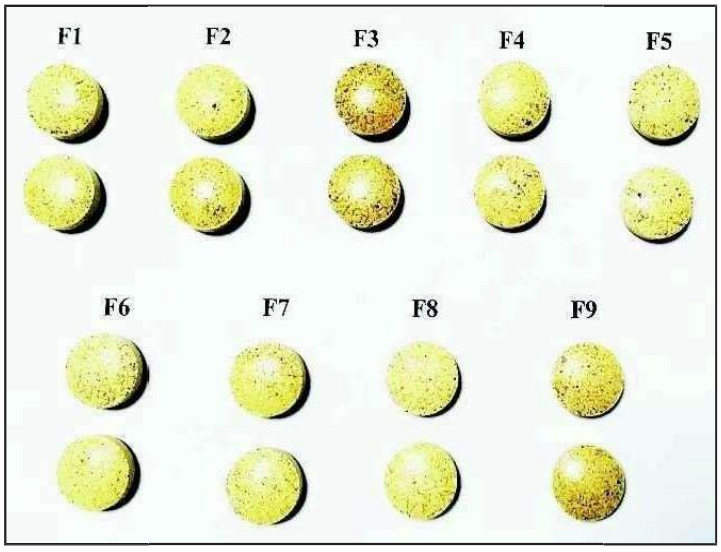

Figure 1: Physical appearance of polyherbal dispersible tablets

The maximum weight variation obtained was ±2.50%, which falls within the acceptable weight variation range, i.e., ±5% hence passed the weight variation test. The hardness of prepared tablets was in the range of 2.94 to 3.02 kg/cm2, which falls within the limit, not more than 3.0 kg/cm2. None of the tablets showed friability value more than 0.90% which is less than the ideal limit, i.e., 1%. Out of all the formulations, formulation PHF-3 has passed the optimized properties, which is less than ideal limits. The polyherbal

formulation (PHF-3) has shown a good uniformity test and the amount content (around 105%) was observed. The formulation PHF-3 has showed the best physical properties i.e., average weight (563.28±7.78mg), weight variation (±2.36%), content uniformity (105.05%), hardness (2.99±0.14kg/cm2), and friability (0.79%) as compared to other formulation containing aqueous root extract of polyherbal formulations (table 3).

Table 3: Physical properties of polyherbal dispersible tablets

Formulation Code	Average weight (mg)	Weight variation (%)	Content uniformity (%)	Hardness (kg/cm^2)	Friability (%)
PHF-1	463.15	±2.34	101.38	2.78±0.13	0.80
PHF-2	462.40	±2.20	100.25	2.91±0.09	0.72
PHF-3	463.28	±2.36	104.05	2.99±0.14	0.69
PHF-4	465.31	±2.71	102.10	3.00±0.12	0.76
PHF-5	460.80	±1.93	098.85	2.94±0.13	0.80
PHF-6	463.63	±2.42	100.80	2.95±0.12	0.70
PHF-7	458.34	±1.22	097.96	2.96±0.16	0.75
PHF-8	463.18	±2.34	101.00	3.02±0.18	0.68
PHF-9	464.13	±2.50	098.68	2.97±0.11	0.78

All values are reported as mean±SD, N=20 Tablets; PHF=Polyherbal formulation Disintegration time

The disintegration time of dispersible tablets were evaluated by using two basket rack assembly USP apparatus. Each basket rack assembly consists of 6 glass tubes that are 3 inches long, open at the top and held against 10 mesh screens at the bottom. Tablets were placed in each basket tube and the basket rack was dipped in the 1-L beaker filled with acidic buffer (pH 1.2) solution at the adequate temperature (37±2°C) maintained throughout the study (Table 4).

Dispersion time

The dispersion time of polyherbal dispersible tablets was observed by placing 2 tablets in 100 ml of water in a beaker with gently stirred until the completely dispersed. A smooth dispersion was obtained by passing through a sieve screen with a nominal mesh aperture of 710µm (sieve no. 22). The study observed that the PHF-3 shows best dispersion time because of it took only 2 min for complete dispersion (Table 4).

The in-vitro disintegration and dispersion time performed in acidic buffer (pH 1.2) for the polyherbal dispersible tablet for all formulations (PHF-1 to PHF-9) were evaluated and recorded that the PHF-3 took only 01.10±0.10 min for complete disintegration and 2.00±0.45 min for apparent dispersion. The PHF-3 rated as best formulation, because of it fulfils all the specification mentioned in IP. It shows lowest disintegration and dispersion time as comparison to other formulation and also shows optimum hardness and minimum friability.

The stability study of polyherbal dispersible tablets carried out for three months at different IP standard condition acceptable for pharmaceutical preparation. The optimized polyherbal formulations were subjected to accelerated stability studies at three different temperature and relative humidity for 3 months. The formulation PHF- 3 shows considerable stability study at the mentioned condition and the result was reproducible even after 3 months stability study (Table 5).

Table 4: Disintegration and dispersion time of the polyherbal dispersible tablet

Formulation Code	Disintegration Time (Min)	Dispersion Time (Min)
PHF-1	01.08±0.62	2.18±0.82
PHF-2	01.45±0.28	1.30±0.60
PHF-3	01.10±0.10	1.00±0.45
PHF-4	01.00±0.45	2.00±0.78
PHF-5	01.18±0.51	1.50±0.65
PHF-6	01.55±0.60	1.24±0.58
PHF-7	01.15±0.55	2.25±0.80
PHF-8	01.06±0.70	2.55±0.71
PHF-9	01.50±0.58	2.00±0.82

All values are reported as mean±SD (n=3 measurements)

Table 5: Stability data of the polyherbal dispersible tablet (PHF-3)

Time	% Drug content at different storage conditions		
	25°C & 60% RH	30°C & 65% RH	40°C & 75% RH
1 month	88.92	89.10	89.30
2 months	89.20	88.86	88.92
3 months	89.34	88.95	87.67

4. CONCLUSION

In conclusion, kidney disorders pose a significant health challenge in contemporary society, with various toxic xenobiotics posing a threat to renal function. Traditional Indian medicine offers a rich source of potential treatments for kidney diseases, with numerous formulations and single drugs historically used for their nephroprotective properties. However, many of these remedies lack comprehensive metabolite profiles and mechanistic insights. In this study, a novel polyherbal formulation was developed, combining extracts from *Rheum emodi, Boerhaavia diffusa, Crataeva nurvala, and Nelumbo nucifera,* all known for their nephroprotective effects. This comprehensive approach enhances our understanding of the formulation's nephroprotective potential and lays the groundwork for further research into effective treatments for kidney disorders.

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