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AYURVEDIC MANAGEMENT OF PRIMARY NEPHROTIC SYNDROME

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Abstract: ***Background:*** Primary nephrotic syndrome is responsible for 12% of the causes of chronic kidney disease and up to 20% of end-stage renal disease. Patients often require cortico-steroids to get remission, yet many patients either show relapse after remission or do not respond to it. The better alternative is, however far from established. ***Objectives:*** This study was performed to determine the effectiveness of the multi-modal Ayurvedic treatment in the patients of nephrotic syndrome. ***Methods:*** This is an observational study on 20 patients, performed with *vardhamana pippali* first 2 weeks followed by mild *virechana karma* with *erandasneha*. After *virecana*, patients were treated with oral Ayurvedic preparations for next 2 weeks. Patients were kept on Ayurvedic preparations except *pippali* for one year. Cortico-steroids (prednisolone) and immunosuppressive drugs (Cyclosporin) were stopped within the main assessment period. Patients were assessed symptomatically and on the basis of laboratory investigations i.e. serum albumin, serum cholesterol and albuminuria after completion of 4 weeks treatment. Patients were assessed every 2 months as follow up with a final assessment after the 12 months follow-up period. ***Results:*** Serum albumin was increased by 12.78% while total cholesterol level was decreased by 18.56%. Albuminuria was increased after the 4 weeks treatment may be because of discontinuation of steroids. However it was decreased by 80.28% after the 12 months follow-up without consumption of steroids or immunosuppressive drugs. These changes were statistically significant. Symptomatic betterment was also observed during the follow-up period. No any unwanted effects were noted during the study period.

Keywords: Ayurvedic Treatment, Primary nephrotic syndrome; *Vardhamana pippali.*

INTRODUCTION

Nephrotic syndrome is a pathological condition of glomeruli in the kidney results from increased permeability of glomerular basement membrane to plasma protein and characterized by excessive proteinuria, hypo-albuminemia, hypercholesterolemia and edema. It is a disease syndrome responsible for approximately 20% of all causes of end-stage kidney disease (ESRD).[1-2]

Disease burden: Nephrotic syndrome is found in every age, irrespective of gender and race. However prevalence is more in adults in comparison to children with a ratio of 26:1. Males are more prone than females with a ratio of 2:1.[3] Nephrotic syndrome has an incidence of three new cases per 100000 each year in adults all over the world.[4] Idiopathic nephrotic syndrome is responsible for approximately 12% of all causes of Chronic kidney disease (CKD) and up to 20% of ESRD in children.[5] One of the primary nephrotic syndrome, Focal Segmental Glomerulo Sclerosis (FSGS) has a high recurrence rate following kidney transplantation (30-40%) and is the most common recurrent disease leading to allograft loss.[6]

Current treatment and its limitations that require to establish safe and alternative regimen: Treatment strategies for NS in conventional medicine include high dose prolonged corticosteroid therapy and other immunosuppressive agents, which all carry significant side effects. Failure of the conventional treatment in achieving remission, frequently results in to progression towards ESRD with its associated costs, morbidities, and mortality. Many patients, however, relapse when the cortisone is tapered off or stopped. They remain in remission for several weeks following discontinuation of treatment but develop frequent relapses. If relapses occur 4 or

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more times in any 12-months period, these patients are referred to as having frequent relapsing nephrotic syndrome (FRNS).[7] Steroid dependant, and frequent relapsing nephrotic syndrome patients are at increased risk of developing complications of nephrotic syndrome and complications from frequent use of steroids and other immunosuppressive agents. Failure to respond to steroid treatment has important ramifications for the risk of developing progressive renal failure later in life. In a multicenter evaluation of 75 cases with NS, it was found that within 5 years after diagnosis, 21% had developed ESRD, 23% had developed CKD, and 37% had developed persistent proteinuria, whereas only 11% remained in remission.[8] Patients often require immune-suppression to achieve remission, yet many patients either relapse after remission or are resistant to therapy.[9-10] The better regimen for "frequent relapsers" and "steroid dependent" patients is, however not yet established. Therefore this is need of time to find and establish scientifically a safe regimen for this kind of disease.

Nephrotic syndrome in ayurveda: Nephrotic syndrome is not directly mentioned with a name in the Ayurvedic classical text books. Because of main characteristic features of albuminuria with hyperlipidemia associated with oedema it may be included under the title of *prameha* (a disease of urinary system with altered composition, frequency and quantity of urine). Albuminuria makes urine concentrated, viscid or dense. These features can be correlated with *sandrameha* a subtype of *prameha*.[11] According to ayurveda, *kapha vata* dominating *tridosha* as well as *rasa, mutra, udaka, ojas* are the components get vitiated in this disease.[12] Any disease even if it is not described in ancient text can be managed by applying the fundamental principles related to pathogenesis and treatment in Ayurveda. On this basis nephrotic syndrome indicates the aggravation of *kapha dosha* along with vitiation of *rasadhatu, ojas, Mutra* and *udaka* involving *mutravaha srotas* and *udakavaha srotas*. Ayurveda is a medical system using complex treatment approaches. Combination of different treatment elements exerts synergistic effects and is benevolent for the outcome. But to date, no clinical study on nephrotic syndrome has been performed which has taken the multidimensional approach of Ayurveda as a complex and whole medical system into account. Therefore we have selected the multi-modal ayurvedic treatment in the management of nephrotic syndrome.

OBJECTIVES

Primary objective of this study is to determine the effectiveness of the multi-modal ayurvedic treatment in the patients of nephrotic syndrome.

This treatment is being used in the patients of nephrotic syndrome since a long time in our P D Patel Ayurveda Hospital, Nadiad (Gujarat) with good outcomes. However the results have never been analyzed critically. We could not find a single scientific publication on Ayurvedic approach in the treatment of Nephrotic syndrome which may promises a potentially effective and safe measure for the disease. Therefore this study planned with aimed to measure the effect of the treatment on modern parameters.

MATERIALS AND METHODS

Patient-selection:

All patients meeting the inclusion criteria (see below) were selected.

Criteria for inclusion:

1. Adult nephrotic patients, more than 18 years of age.
2. Diagnosis of idiopathic nephrotic syndrome.

Criteria for exclusion:

1. Patients with an eGFR (glomerular filtration rate) less than 30 ml/min/1.73m2
2. Patients of idiopathic nephrotic syndrome having complications like thromboembolism, cardio-vascular diseases, ESRD were excluded.
3. Patients with other renal diseases (e.g. diabetic nephropathy, renal vascular disease) that would interfere with interpretation of the study.
4. Patients with co-morbid conditions that would interfere with completion of the trial (malignancies, CHF, recent myocardial infarction).
5. Female patients having pregnancy or lactating period.

Study period:

Patients fulfilled the inclusion criteria were treated as in-patients up to the 4 weeks of main assessment. During the follow-up, patients were

treated as out-patients. Minimum follow-up period was of 12 months. During follow-up patients were observed clinically for signs, symptoms and laboratory findings every 2 month.

Therapy:

All patients were treated with:

A. *Vardhamana pippali*[13]: Fine powder of *pippali* (*Piper longum* Linn.) was given in increasing and tapering dose-pattern. In this pattern 1 g powder of *Piper longum* was given twice with honey on the first day. Every day the dose was increased by 1 g eventually to reach to 5 g twice daily. The dose of 5 g was kept for 5 days and then tapered down 1 g every day to finally reach 1 g again. This took 13 days. On the 14th day we performed mild *virecana* (purgation) with *eranda sneha* (oil of the seeds of *Ricinus communis* Linn.). The dose of *eranda sneha* was 30-40 ml according to the patients' *kostha* (frequency and sensitivity of bowels).

B. After the completion of purgation following treatment was given for the next 2 weeks:

1. *Gokshuradi Guggulu*[14] – 1 g, 3 times in a day after food with warm water.
2. *Varunadi kvatha*[15] – 40 ml 2 times in a day after food.
3. *Haritakyadi kvatha*[16] – 40 ml 2 times in a day after food.
4. *Rasayana Churna* (powder of fruit of *Gokshura* - *Tribulus terrestris* Linn. + fruit of *Amalaki* - *Embelica officinalis* Gaertn. + stem of *Guduchi* - *Tinospora coridifolia* Miers. in equal quantities) – 3 g, 3 times a day with water.

C. Patients were kept on following diet during the main assessment period and also in follow-up period.

Breakfast: *Chyavanprashavaleha* (Ayurvedic tonic / medicine to be taken in by licking) – 10 g with 150 ml milk (Amul milk).

Lunch: Boiled mung, barley flour chapatti, mung beans soup, boiled vegetables and rice.

Dinner: Mung beans soup, rice or Khichadi (Indian recepie which contains equal quantity of mung beans and rice), boiled vegetables.

Others: Patients can take fruits (only Papaya and sweet apple), pop rice, and dates if they become hungry during the day period other than lunch, breakfast and dinner. Patients can take 150 ml milk (other than breakfast) in a day, but not to take milk with any above food items. Salts, oily, spicy, heavy to digest items, cheese, paneer, sweets, curd and sour taste were totally restricted.

D. Patients who were on conventional diuretics (e.g. furosemide and spironolactone) were advised to continue initially. The doses of conventional diuretic drugs were modified and eventually stopped according to status of patient and or the reduction in the swelling as well as increase urine output. These were stopped totally within 4 weeks of the main assessment period. The prednisolone was also reduced gradually (as in tapering dose) and stopped totally in all the patients within 4 weeks of the main assessment period.

E. During follow-up period patients were instructed to take all the medicaments except *vardhamana pippali* (because it is a rasayana therapy and it could not be taken without expert supervision and hospitalization) as well as mentioned diet and not to take cortico-steroids or immunosuppressive drugs.

Preparation of medicine:

Ayurvedic medicines were prepared under expert supervision strictly adhering to standard operating procedures (SOP).

Assessment of the result:

All the patients were clinically assessed before and after the treatment. Signs and symptoms were assessed by giving score (Table 1). The grade score of signs and symptoms were prepared by us. Changes in signs-symptoms, total urine output, serum albumin, serum cholesterol, albuminuria, serum creatinine, blood urea and hemoglobin were observed and evaluated with paired t-test. Total urine output in 24 hours (in liters) was measured and assessed initially and periodically (during and after the treatment). The study results were statistically analyzed by using the paired 't' test. The average data recorded at the end of the study was compared with the data recorded at the beginning of the study. A value of $p<0.01$ was considered as statistically significant.

Table 1. Grade score of signs and symptoms.

Signs and symptoms	Grade 0	Grade 1	Grade 2	Grade 3
Oedema	No oedema	Slight puffiness on face	Marked oedema on face and slight oedema on extremities	General Anasarca
General weakness	No weakness	Mild weakness	Moderate weakness	Severe weakness
Loss of appetite	Good appetite	Mild loss of appetite patient still can eat needed quantity which was before the disease	Moderate Loss of appetite patient cannot eat the quantity taken earlier	patient cannot eat the quantity taken earlier and has to be forced to eat
Nausea / Vomiting	Absent	Present	---	---

OBSERVATIONS AND RESULTS

Baseline observations: Total 26 patients with primary nephrotic syndrome were screened. Out of those, 6 patients left the treatment early because of personal reasons not related to the therapy. Overall, 20 patients' data sets were completely recorded.

Mean value of the age was 37 years. Male patients were more than female (14 male patients). Most of the patients have more than three years chronicity. The average value of chronicity of all the patients is 3.45 years. All the patients were taking the steroid therapy. One patient was taking cyclosporine immunosuppressive drug. 11 patients were belonging in to the steroid dependent type of nephrotic syndrome, while nine patients were of frequently relapsing type of nephrotic syndrome. Most of the patients have Focal segmental glomerulosclerosis (6 patients) and Membrano-proliferative glomerulonephritis (5 patients). All the patients have any one of the unwanted effect of the steroid therapy **(Table 2).**

Table 3 and **4** shows effect of the therapy after the completion of main assessment period as well as 12 months follow-up period. Urine output was increased significantly by 168.32% during the main assessment period. Patients during follow up were not at home for whole time and therefore the urine output could not be measured reliably in them, hence not assessed. Oedema, weakness and loss of appetite were decreased by 51.78%, 51.72% and 83.33% respectively after the main assessment period. After the 12 months follow-up period they were improved by 96.42%, 78.75% and 100% respectively. Improvement in all the signs and symptoms was statistically highly significant. Albuminuria was increased by 2.81% and it was statistically insignificant. After the 12 months of follow-up period it was decreased by 80.28% and statistically it was highly significant. Serum albumin was increased by 12.78% while total cholesterol level was decreased by 18.56% after the completion of main assessment period. After the 12 months of follow-up period serum albumin was increased by 62.32% while serum cholesterol was decreased by 34.39% and both the results were statistically highly significant. Albuminuria was increased after the 4 weeks treatment may be because of discontinuation of steroids. However it was decreased by 80.28% after the 12 months follow-up without consumption of steroids or immunosuppressive drugs. Hemoglobin level was increased by 3.77% after

Table 2. Baseline observations of twenty patients.

Characters	Mean value
Age (in years)	37
Sex (Male:Female)	14:06
Chronicity (in years)	03.45
Causes of nephrotic syndrome	**Patients**
Membranoproliferative glomerulonephritis (MPGN)	05
Membranous Nephropathy (MN)	03
Focal segmental glomerulosclerosis (FSGS)	06
Minimal Change Nephrotic syndrome (MCNS)	02
IgM Nephropathy	03
Mesangial proliferative Glomerulonephritis	01
Types of nephrotic syndrome	**Patients**
Steroid Dependent Nephrotic Syndrome (SDNS)	11
Frequently Relapsing Nephrotic Syndrome (FRNS)	09
Unwanted effects of steroid therapy	**Patients**
Moonlike face	14
Low immunity (any of the repeatedly coryzal syndrome, fever, infections or any other signs of lake of immunity)	04

Table 3. Improvement in signs and symptoms after completion of 4 weeks of treatment and follow up.

Signs and symptoms (with n*)	Main assessment period				Follow-up period			
	Mean value		Change in %	*P* value	Mean value		Change in %**	*P* value
	BT*	AT*			6 months	12 months		
Urine output in Liter (20)	0.75	2.02	168.32	< 0.001	The urine output could not be measured reliably in outdoor-patients, hence not assessed.			
Oedema (20)	2.8	1.35	51.78	< 0.001	0.60	0.10	96.42	< 0.001
Weakness (16)	1.93	0.87	51.72	< 0.001	0.62	0.41	78.75	< 0.001
Loss of appetite (12)	1.00	0.17	83.33	< 0.001	0.00	0.00	100	< 0.001

Table 4. Improvement in laboratory investigations.

Laboratory investigation	Main assessment period				Follow-up period			
	Mean value		Change In %	P value	Mean value		Change In %**	P value
	BT	AT			After 6 months	After 12 months		
Albuminuria	3.55	3.60	(-) 2.81	> 0.1	1.15	0.7	80.28	< 0.001
S. Albumin	2.19	2.47	12.78	< 0.001	3.33	3.55	62.32	< 0.001
S. Cholesterol	368.7	300.25	18.56	< 0.001	270.4	241.9	34.39	< 0.001
Hemoglobin	11.4	11.83	3.77	< 0.001	11.93	12.38	08.64	< 0.001
S. Creatinine	1.08	1.00	7.4	< 0.05	0.97	0.87	19.44	< 0.001
Blood Urea	38.7	30.75	20.54	< 0.05	31.65	30.0	22.48	< 0.001

*n-number of patients; BT-Before Treatment; AT-After 4 weeks' (main assessment period) Treatment
**Percentage shows improvement after one year follow-up from initial level (BT).

the main assessment period and 8.64% after the 12 months of follow-up. Serum creatinine and blood urea level was within normal level at initial stage and also found within normal limit during and after the 12 months of study period.

Initially mean value of the consumption of steroid (prednisolone) was 51.5 mg per day. Steroid therapy was stopped in all the patients by tapering dose method within the 4 weeks (main assessment) period. During follow-up period steroid therapy was not given in any of the patient. The improvement in the patient was noted in follow-up period without intake of prednisolone or immunosuppressive drugs.

DISCUSSION

Mean value of 37 years age suggest that this disease occurs mostly in middle aged people in adults. Repeatedly and prolonged use of the steroid therapy in the patients suggests that this disease has steroid dependent or frequently relapsing type of nature. Observation suggests that nephrotic syndrome is a chronic disease, having relapsing nature and more in male patients. Steroids therapy having some remission effect on this disease, but relapse also occurs in the most of the patients. Most important *dhatus* i.e. *rasa, udaka, rakta, mutra* and *oja* are involved. *Bala* (strength as well as immunity) depends upon the *oja* according to Ayurveda. Therefore in the patients of idiopathic nephrotic syndrome, physical strength was mostly low according to the *atura bala pramana pariksha* of ayurvedic classics.

The signs and symptoms of the nephrotic syndrome i.e. oedema, loss of appetite and weakness were improved in all the patients and results were highly significant. The urine albumin level was increased in some patients because initially they were taking prednisolone in high dose, which was totally stopped in the main assessment period (within 4 weeks). In the follow-up period, all the patients got significant improvement in the level of urine albumin, serum albumin and lipid profile even after stopped the steroid therapy. Some patients also got the benefit in glycosuria. Most probably, this glycosuria may be due to steroid therapy.

There is evidence in the literature that nephrotic syndrome may be a consequence of a primary glomerular defect, circulating factors, or an immunological abnormality. Primary glomerular defects mostly due to the proteins which creates the mutations in genes encoding podocyte and GBM proteins.[17-18-19-20] In circulating factors, Protein A immune-adsorption is responsible for the

primary nephrotic syndrome. Immunological abnormalities, mostly auto-immune process also creates the primary nephrotic syndrome. All these factors can be concluded under the broad heading of *ama* according to ayurveda. Immunological abnormalities can be correlated with *balabhransha* (one of the feature of *ama*) according to ayurveda. *Oja* (extreme qualities of all the *dhatus*) is responsible for appropriate *bala*. *Rasayana* therapy increases the quality of all the *dhatus*. So *rasayana* therapy increases the proper *bala* (immunity according to modern medicine) in the body. *Vardhamana pippali rasayana* is one of the rasayana therapies which not only increase quality of the tissues but also decrease the *ama* factors by its *ama pachana* properties. Recent researches indicate that *Pippali* (fruits of *Piper longum*) has anti-inflammatory action[21-22]. Extract of *Piper longum* fruits have been shown to posses various activities like Bio-availibity enhancer, immune-modulatory effect, antiasthamatic and hepato-protective activity.[23] *Varunadi kvatha* having the *kapha-vata shaman* and *meda-mutradoshahar* properties. Though all the *three doshas* as well as all the *dushyas* are involved in the disease, *kapha* and *vata* are more aggravated in this disease. According to Ayurvedic principles of management of the disease, tissue damage can be prevented and repaired by *rasayana* drugs because they have the capability to improve qualities of tissues and hence increase resistance of the tissues. *Goksuradi guggulu* and *rasayana churna* (combined Ayurvedic preparation) is *rasayana* for *mutravaha srotas* and it has also properties for mitigation of *kapha* and *vata*. *Haritakyadi kvatha* is indicated in *mutrakricchra* and *prameha roga*.

Limitations of the Study

However, the outlined treatment protocol has some limitations. It cannot be introduced in patients having serious complications because management selected in this study is possible only if patient is fully conscious. Study with larger number of patients will generate more statistical evidence. Moreover, the inclusion of further assessment criteria like pre- and post-treatment renal biopsies may be helpful to give some clues on histological changes.

CONCLUSION

Total 20 patients have completed the treatment with minimum 12 months of follow-up. Signs and symptoms i.e. oedema, loss of appetite, weakness and vomiting were improved significantly and during the follow-up period no any sign reoccurred. Significant improvement was also noted in all the laboratory investigations. Serum albumin was increased while serum cholesterol and albuminuria were decreased after the completion of 12 months follow-up period. Serum creatinine and blood urea were found within the normal limit in entire study period. No steroid therapy was given after the completion of main assessment period. No any unwanted sign noted during the study period. *Vardhamana pippali* and other ayurvedic preparations used in this study are safe and effective in the patients of nephrotic syndrome. This therapy is effective and probably safe for prolonged period in the patients of steroid dependent and frequently relapsing type of primary nephrotic syndrome without taking cortico-steroids or immunosuppressive drugs.

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Conflict of Interest: Nil

References

1. **ISKDC:** Primary nephrotic syndrome in children: clinical significance of histopathologic variants of minimal change and of diffuse mesangial hypercellularity: A Report of the International Study of Kidney Disease in Children. *Kidney Int* **1981**; 20(6):765-771.
2. **Eddy A A, Symons JM**. Nephrotic syndrome in childhood. *Lancet* **2003;** 362(9384):629-639.
3. **Borrego R, Jaime Montero C, Orlando**. *Nefrología: Fundamentos de medicina*; Cuarta edition; Corporación para investigaciones biológicas **2003**; 340.
4. **Lach F.** Thromboembolic complications in the nephrotic syndrome: coagulation abnormalities, renal vein thrombosis and other conditions. *Postgrad Med* **1984**; 76:111-4, 116-8, 121-3.
5. **Fine JL, Grzybicki DM, Silowash R, Ho J** *et al*. Evaluation of whole slide image immunohistochemistry interpretation in challenging prostate needle biopsies. *Hum Pathol* **2008**; 39: 564-572.
6. http://medicine.med.nyu.edu/nephrology/node/610#sthash.aSOq4BAc.dpuf. assessed on 28th February 2014 at 15:00 IST

7. **Schulman SL et al**. Predicting the response to cytotoxic therapy for childhood nephrotic syndrome: superiority of response to corticosteroid therapy over histopathologic patterns. *J Pediatr* **1988**; 113 (6):996-1001.

8. **The Southwest Pediatric Nephrology Study Group**; Focal segmental glomerulosclerosis in children with idiopathic nephrotic syndrome: A report of the Southwest Pediatric Nephrology Study Group. *Kidney Int* **1995**; 27:442-49.

9. **Waldman M, Crew RJ, Valeri A,** *et al***.** Adult minimal-change disease: clinical characteristics, treatment, and outcomes. *Clin J Am Soc Nephrol* **2007**; 2:445–453.

10. **Palmer SC, Nand K, Strippoli GF**. Interventions for minimal change disease in adults with nephrotic syndrome. *Cochrane Database Syst Rev* **2008**; CD001537.

11. **Agnivesa, Caraka, Dradhabala**. *Caraka Samhita*; Nidanasthana; Pramehanidana Adhyaya 04/15, edited by Vaidya Jadavaji Trikamji Acharya. 2nd edition, Chaukhamba Samskrit Samsthan, Varanasi, **1990**

12. **Agnivesa, Caraka, Dradhabala**; *Caraka Samhita*; Cikitsasthana; Pramehacikitsa Adhyaya 06/08, edited by Vaidya Jadavaji Trikamji Aacharya. 2nd edition, Chaukhamba Samskrit Samsthan, Varanasi, **1990**.

13. **Agnivesa, Caraka, Dradhabala**; *Caraka Samhita*; Cikitsasthana; Rasayana Cikitsa Adhyaya; 1, 3rd Pada, Shloka 36-40, edited by Vaidya Jadavaji Trikamji Acarya. 2nd edition, Chaukhamba Samskrit Samsthan publication, Varanasi, **1990**; 494

14. **Sharangadhara**, *Sharangadhara samhita*; madhyama khanda, adhyaya 7/84-87. gujarati translation by Rasiklal Parikh; 3rd edition, Tribhuvandas K Thakkar publication **1971**; 310.

15. **Sharangadhara**, *Sharangadhara samhita*; madhyama khanda, adhyaya 2/130-131. gujarati translation by Rasiklal Parikh; 3rd edition, Tribhuvandas K Thakkar publication **1971**; 235.

16. **Sharangadhara**, *Sharangadhara samhita*; madhyama khanda, adhyaya 2/103; gujarati translation by Rasiklal Parikh; 3rd edition, Tribhuvandas K Thakkar publication **1971**; 228.

17. **Shih NY** *et al*. Congenital nephrotic syndrome in mice lacking CD2-associated protein, *Science* **1999**; 286 (5438):312-15.

18. **Boerkoel CF** *et al.* Mutant chromatin remodeling protein SMARCAL1 causes Schimke immuno-osseous dysplasia. *Nat Genet* **Epub 2002 Jan 22;** 30 (2):215-20..

19. **Zenker M** *et al.* Human laminin beta2 deficiency causes congenital nephrosis with mesangial sclerosis and distinct eye abnormalities. *Human Mol Genet* **2004**; 13 (21):2625-32.

20. **Morello R, Lee B.** Insight into podocyte differentiation from the study of human genetic disease: nail-patella syndrome and transcriptional regulation in podocytes. *Pediatr Res* **2002**; 51 (5):551-58.

21. **A. Kumar et.al**. Antiinflammatory activity of piper longum fruit oil. *Indian Journal of Pharmaceutical Sciences* **2009;** 71 (4):454-456.

22. **Mamtakumar** *et.al*, Anti-inflammatory activity of two varieties of pippali, *AYU* **Apr-Jun 2012;** 33 (2):307-310.

23. **Chauhan Khushbu, Solanki Roshni, Patel Anar, Macwan Carol, Patel Mayuree**. Phytochemical and therapeutic potential of piper longum linn : A review. *International Journal of Research in Ayurveda and Pharmacy (IJRAP)* **2011**; 2 (1):157-161.

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