A urinary tract infection (UTI) is an infection of the urinary tract and most commonly occurs in the bladder. It is the second most common illness in middle-aged women. UTI is caused by bacteria that enter the urinary tract. Many bacteria can cause UTI, but Escherichia coli is the most common cause. Other bacteria can also cause UTI, such as Klebsiella, Pseudomonas, Enterobacter, Proteus, Staphylococcus, Mycoplasma, Chlamydia, Serratia, and Neisseria spp. However, these bacteria are less common than E. coli. In addition, fungi (Candida and Cryptococcus spp) and some parasites (Trichomonas and Schistosoma) also cause UTI. Schistosoma causes other problems, such as bladder infections or infection with other types of complications. The complications of UTI are often asymptomatic, and a patient may not notice its presence before treatment. Therefore, the symptoms of UTI may not be severe, and the patient may not notice them until a treatment is started. The symptoms of UTI include burning, frequency, urgency, and dysuria. An open-label study was conducted to evaluate the safety and efficacy of Unex® capsules in patients with UTI. Patients aged 18 to 70 years were enrolled in the study, and the study was done according to good clinical practices (GCP). The study was approved by the Institutional Ethics Committee (IEC). A dose of 2 capsules BID was given to the patients for 8 weeks. The results of the study were analyzed to assess the efficacy and safety of the treatment. The results revealed that the treatment was effective and safe. The treatment was effective in resolving symptoms of UTI and was safe without any adverse effects. Therefore, Unex® capsules can be used as an alternative to prescription medications for the treatment of UTI.
All investigational medicinal products (IMP) were supplied by sponsored company Unijules Life Sciences Ltd with appropriate labeling and packing. Quality assurance audits were also conducted during the study for compliance with protocol, source data verification, patient recruitment etc, by the company. All patients of urinary disorders attending OPD of the hospital were selected and included in the treatment period with following inclusion and exclusion criteria.

2.1 Inclusion criteria
All patients aged between 18 to 70 years of age must have a diagnosis of Dysuria or painful discharge of urine with burning sensation. Urgency or a strong urge to pass urine with recurrent urination. Hesitancy or a feeling of inability to pass urine completely. Pain and discomfort of lower abdomen. Hematuria or bloody urination with foul smell. One positive dipstick urine test positive either for leukocyte esterase or nitrates or have a urinalysis with > 5 wbc/hpf. A pre-treatment clean-catch midstream urine culture with ≥ 104 CFU/mL of a bacterial organism, Voluntary able to understand the nature and purpose of the study, including the risks and adverse effects and with intent to cooperate with the researcher and act in accordance with the requirements of the entire protocol, which was confirmed by signing the consent.

2.2 Exclusion criteria
Patients with significant diseases other than urinary tract disorders were excluded. Patients with a significant disease (defined as a disease which in the opinion of the investigator may either put the patient at risk because of participation in the study or a disease which may influence the results of the study or the patient's ability to participate in the study). Patients with clinically significant abnormal baseline hematology, blood chemistry or urinalysis, if the abnormality defines a disease listed as exclusion criterions were excluded. Female patients who are pregnant or lactating, Patients with known polycystic kidney disease, Patients on permanent renal replacement therapy (hemodialysis or peritoneal dialysis), Patients with history of kidney transplantation, were excluded from the study.

2.3 Assessment of efficacy
The primary efficacy outcome was Clinical response, the resolution of Urinary disorders like burning micturition, dysuria, hesitancy and frequency of urination, Abdominal pain and signs and symptoms at post-therapy compared with those at start of study; Microbiological response, the eradication at post-therapy of infectious organism identified at start of study. Secondary efficacy variables were Overall clinical response, described as cured, improved, or failed; incidence of adverse events throughout the study; Change in clinical laboratory tests and physical examinations from start of study to post-therapy.

Safety was assessed by the changes observed in essential biochemical investigations i.e. LFT, CBC and hazards symptoms observed during the treatment course w.r.t. palatability, convenience and amount of rescue medications utilized by the patient for any untoward sign and symptoms during the therapy.

2.4 Study drug
The study drug Unex capsule was a FDA approved product with a combined aqueous extract of Tribulus terrestris and Boerhavia diffusa in a specific technology based dosage form of pellets capsule of 0.470mg pallets. The dose was 2 capsules before meal two times a day was decided for the study which derived from the results of in-house pilot study.

2.5 Study procedure
This study was a prospective, single blind study involving patients with urinary disorders. The study incorporated a matched pairs design. Each patient has received a single treatment of investigational product (UNEX). The goal was to enroll approximately 200 patients in order to have 175 patients to provide data for analysis. Patients selected from the OPD were examined for the adherence to the above mentioned inclusion and exclusion criteria and provided with details about the study, study drug, its effect, dosing schedule etc and asked for signing a written informed consent form. Screening period of 2 days was kept during which patients were checked for all hematological, biochemical and physical tests for analyzing its adherence with the protocol, appropriateness of the patients for further treatment period and also to check safety parameters. Parameters like LFT, KFT etc were done and those who find eligible for further study were enrolled for further treatment period of eight weeks.

It was aimed to enroll at least 175 patients in the study in order to have 150 patients’ data for final analysis. Follow-up visits were scheduled after 2, 4, 6 and 8 weeks and during each visit vital signs and severity of symptoms score i.e. from 0 to 3 (Normal, Mild, Moderate, Severe as defined in protocol) for symptoms like hesitancy, burning micturition, dysuria, abdominal pain etc were noted. Urine examination for routine and microscopic were performed in each visit. Checking of daily diary, use of rescue medications etc were noted and documented during each visit. A window period of +/− 2 days was allowed for the visit. All adverse events were noted and recorded about nature and severity of the symptom, onset action, time to resolution of symptom. Patients were allowed to withdraw from the study at any time and any stage of the study. All data were compiled and analyzed by using appropriate analytical test i.e. paired t test for grouped data and unpaired t test for comparing ungrouped data of group I and group II.

3. RESULTS AND DISCUSSION
In the present clinical study, total 188 patients were screened out of which 179 patients were enrolled (according to adherence with inclusion and exclusion criteria) for the further study and out of them 171 patients have completed their 8 weeks treatment period, (as 8 patients have discontinued the study due to non-follow up after 2 weeks of treatment)

The efficacy of UNEX has been evaluated in 171 cases of Urinary disorders. Patients who presented with various symptoms of Urinary disorders, Hematological Examination: The TLC, DLC and estimation of Hb%, Blood urea and Serum creatinine were done before, during and after the completion of therapy. No significant changes were observed in TLC, DLC and Hb% after treatment with UNEX. Similar observations were also made in blood urea and serum creatinine level. This suggests that the drug has no adverse effect on renal function.

In case of burning micturition (Graph 1) significant results were observed after 4th week of treatment and highly significant results were observed after 6th and 8th week of treatment. In case of hesitancy and frequency of micturition (Graph 2) significant results were observed after 8th week of treatment. And in case of abdominal pain (Graph 3) associated with urinary disorders, significant results were observed after 2nd, 4th, 6th and 8th week of treatment. In case of dysuria (Graph 4) significant results were observed after 2nd, 4th, 6th and 8th week of treatment. In Urine analysis (Table 1) also significant results were noted in case of bacteriuria, microscopic evidences and haematuria after 4th and 8th week of treatment. No any adverse or unwanted observations were noted during and after the completion of 8th week treatment duration.
Urinary disorder is more common in females. In women about 50% - 80% of women acquire at least one urinary disorder during their lifetime which is mostly uncomplicated cystitis. The annual incidence of pyelonephritis was approximately 28 per 10,000 women. Urinary disorder is rare in young men. In the elderly age group, benign prostatic hyperplasia has been implicated as a common predisposing factor for urinary disorder. In men, a single episode of urinary disorder has to be investigated particularly if the patient is in the younger age group[13,9]. In this study out of 171 patients treated, 98 were females and 73 were males.

Certain people are more likely to get urinary disorders. Women tend to get them more often because their urethra is shorter and closer to the anus. Elderly people (especially those in nursing homes) and people with diabetes also get more urinary disorders. Cystitis in children can be promoted by abnormalities in the urinary tract. Therefore, children with cystitis, especially those under age 5, deserve special follow-up to prevent later kidney damage. Bacteria that are normally found in the gastrointestinal tract, such as Escherichia coli, cause most urinary tract infections. Other bacteria that can cause urinary tract infections include Staphylococcus saprophyticus, Proteus, Klebsiella and Enterococcus[10,11].

In recent years, an increasing number of bladder infections in both men and women have been linked to two sexually transmitted organisms; Chlamydia trachomatis and Mycoplasma genitalium. Women are more prone to urinary tract infections because the tube running from the bladder to the outside (the urethra) is much shorter than in men. Because the urethral opening is relatively close to the anus in women, bacteria that are normal present from the colon can easily contaminate the female urethra. A urinary tract infection in young women is often associated with increased sexual activity[12,13].

In men, however, a bladder infection is almost always a symptom of an underlying disorder and a cause for concern. Often the infection has migrated from the prostate or some other part of the body, signaling problems in those locations. Or it may indicate a tumor or other obstruction is interfering with the urinary tract. Chronic kidney infections in children are sometimes caused by a structural problem that allows urine to flow back from the bladder to kidneys (reflux). UNEX capsule is a powerful Diuretic and Urinary Antiseptic. The herbs used in UNEX are time tested for removing stone from urinary system.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Unex</th>
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<tbody>
<tr>
<td>Bacteriuria</td>
<td>Present 90, 80, 50, 20</td>
</tr>
<tr>
<td>Absent 81, 91, 121*, 151*</td>
<td></td>
</tr>
<tr>
<td>Present 70, 55, 45, 10</td>
<td></td>
</tr>
<tr>
<td>Microscopic hematuria</td>
<td>Present 23, 18, 12, 0</td>
</tr>
<tr>
<td>Absent 101, 116, 126, 161**</td>
<td></td>
</tr>
<tr>
<td>Microscopic infections (Microscopic evidence)</td>
<td>Present 148, 153, 159*, 171**</td>
</tr>
<tr>
<td>Initial 90, 80, 50, 20</td>
<td></td>
</tr>
<tr>
<td>2 W 8 W</td>
<td></td>
</tr>
<tr>
<td>4 W 8 W</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Microscopic parameters of urine

**Highly significant results after 4th and 8th week of treatment

**Significant results after 4th week of Tt. And *** highly significant after 6th and 8th week of Tt.
Boerhavia diffusa (Boerhavia diffusa) and 1 g Gokhru (Tribulus terrestris). Tribulus terrestris contain marman as principle constituents. It is diuretic drug useful in urolithiasis, dysuria and kidney dysfunction. It is very useful in disease of genitourinary tract.

It is used as diuretics, cooling, useful in painful micturition, calculus affections, and urinary discharges in gout and kidney diseases, inhibition of tyrosinase, urolithiasis and crystalluria. It helps to maintain efficient kidney and urinary discomfort and reduces renal discomfort[^1][^10].

The diuretic action of Boerhavia diffusa has been studied and validated by scientist in several studies, which helps to explain its long history of use in various kidney and urinary conditions. It is used for gall bladder pain and stones, urinary tract and renal disorders and calculi and for cystitis[^16][^17].

4. CONCLUSION

UNEX Capsules was found to be very effective in symptomatic improvement of UTI within 2 weeks in terms of dysuria, Abdominal pain and burning micturition. Only in case of frequency and hesitancy of micturition it takes 8 weeks for significant improvement. It was also effective in changing urinary pH to alkaline medium which focuses on its affectivity as an alkalizer. It was effective in preventing recurrence of urinary disorder as no recurrence is observed after 4 week of completion of treatment. It also has potentiating antibacterial activity as seen by the decrease in bacterial colony count and absence of pus cells in the urine. No side effects were seen with drug. There was good response in terms of compliance. Considering the excellent results of the clinical trial, it can be concluded that UNEX is effective in the treatment of Urinary disorders like simple burning micturition, UTI, cystitis and chronic prostatitis, without producing any undesirable side effects.

In cases of chronic urinary tract infections, it may be useful if used for long term prophylaxis.

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References: