The Cancer Research Review
Online ISSN 3006-9343
Print ISSN 3006-9335

THE CANCER RESEARCH REVIEW
Online ISSN 3006-9343
Print ISSN 3006-9335
http://the-crr.com/index.php/Journal
Name of Publisher: DIVINE KNOWLEDGE INSTITUTE
Vol. 2 , Issue. 4 (2024)

EVALUATION OF INULA CRITHOMOIDES, ASTRGALUS ADSCENDENS AND HELIOTROPIUM EICHWALDII AGAINST DIARRHOEAL AND URINARY TRACT INFECTIOUS BACTERIAL PATHOGENES

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ABSTRACT

The aim of this study was to investigate the phytochemical composition and antibacterial properties of three medicinal plants i.e., *Inula crithomoides*, *Astragalus adscendens* and *Heliotropium eichwaldii* used locally against diarrhoeal and urinary tract infectious diseases obtained from the hilly areas of district Karak KPK Pakistan. Using normal protocols, a preliminary phytochemical screening of the aforementioned plants extracts in ethyl acetate, chloroform, n-hexane, and distilled water showed the presence of several components, including alkaloids, flavonoids, tannins, and saponins. The plants were found to be rich in alkaloids because each fraction of each plant has shown the presence of alkaloids. Then the four fraction of each plant were subjected to evaluate them against the selected diarrhoeal and urinary tract infectious bacterial pathogens like *E.coli* (ATCC), *E.coli* (MDR), *P.aeruginosa* (ATCC), *P.aeruginosa* (MDR), *Salmonella sp, Shegilla sp* and *MRSA* by using ager well diffusion method. All of these plants extracts were found

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to be moderately inhibitory against these pathogens except the n-hexane and chloroform fraction of *Heliotropium eichwaldii* which have shown strong inhibition against *salmonella* specie. Thus, the use of herbal plants is the primary source of medications used in traditional medicine to treat various diseases.

Keywords: Phytochemical; herbal plants; diarrhoea; alkaloids; pathogens

INTRODUCTION

Diarrhoea is one the major health problems, threatening the rising world. The diarrhoeal infection causes a repeated loose and watery stools, abdominal ache and loss of essential electrolytes which may lead to mortality [1, 2]. On the other hand, urinary tract infections are caused due to the bacterial attack on the inner lining of urinary tract. Mostly females are at high risk as compare to males and they frequently infected due to their urethral physiology/anatomy (shorter urethra and its closeness to anal area) [3, 4]. The effect of these two types of infections as such that; the diarrhoea can infect people of all ages but children with the age less than five years are harshly affected by it [5]. While there is still confusion in the exact velocity of urinary tract infections and shows variance with the age and gender of the patients. Approximately 80% of the females and 20% of the males have the chance of UTIs such as pyelonephritis and cystitis at least once in their babyhood [6, 7]. The economic point of view shows that the United States spends an amount of $6 billion annually on food borne diseases, majority of which cause diarrhoea [8] and similarly more than 7 million patients with UTIs visits health care centers and demand for more than one billion US dollars on overall health care expenses [9, 10]. The bacterial pathogen such as *Escherichia coli* is both common to diarrhoea and UTIs [11, 12].

Pseudomonas aeruginosa has been found in the stool cultures of the patients of nosocomial diarrhoea and is one of the common causes of Catheter-associated UTI (CAUTI) and is responsible for 40% of nosocomial infections [13, 14]. Salmonellosis caused by *Salmonella* (non-typhoidal) results in the abdominal pain,

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diarrhoea, nausea and sometimes vomiting [15]. *Shigella* is Gram negative, non-motile, rod-shaped bacteria, causing human shigellosis and dysentery, which results in acute diarrhoea with the presence of blood in the faces [16]. Methicillin-resistant *S. aureus* is also one of the dangerous agents of urinary tract infections resulted due to the use of catheter [17]. In the present time people are using many antibiotics indiscriminately in treating different infectious diseases like malaria, tuberculosis, diarrhoeal diseases, urinary tract infections etc. and has resulted in another key health problem that is the antimicrobial resistance [18].

Multidrug-resistant (MDR) infections caused by bacteria have increased the rate of deaths, longer stay in hospitals, higher expenses on health care and treatment. So these circumstances have substantially threatened the current antibacterial evaluation [19]. From the beginning and still plants are considered to be the rich sources of valuable and safe medicines; recently the researchers have focused on plants that show activity against microbes, so this is why plants are still considered as the core for new medications to treat infectious diseases [20]. The reason for the plants importance is that they contain essential phytoconstituents such as alkaloids, saponins, flavonoids and tannins and these phytochemicals have been determined to have therapeutic values [21].

MATERIALS AND METHODS

PLANTS COLLECTION AND EXTRACTION

The plants *Inula crithomoides*, *Astragalus adscendens* and *Heliotropium eichwaldii* were collected from the hilly areas of district Karak KPK Pakistan and were identified. The plants were washed carefully three times with tap water and then two times with distilled water, dried under shad, powdered and were extracted with methanol. Furthermore the methanolic extract of each plant was successively fractioned with *n*-hexane, chloroform, ethyl acetate to get *n*-hexane, chloroform, ethyl acetate and water soluble fractions or extracts respectively with the help of separating funnel. All the four extracts of each plant were

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phytochemical analyzed and then subjected to antibacterial evaluation against selected diarrhoeal and urinary tract infectious bacterial pathogens.

QUALITATIVE ANALYSIS OF PHYTOCHEMICALS

Before the antibacterial evaluation, these plants were subjected to the phytochemical analysis so as to find out the presence of medicinally important phytochemicals such as alkaloids, flavonoids, tannins and saponins.

ALKALOIDS

20 mg of the plant extract or fraction was dissolved in 1.5 ml of methanol, then filtered and 2% of HCl was added to filtrate and was heated on boiling water bath, then treated with Mayor's reagent. The sample was then observed for the presence of creamy or yellow colored precipitates or turbidity for presences of alkaloids [22, 23].

FLAVONOIDS

Dissolved 20 mg of the plant extracts or fraction in 1.5 ml of ethanol, then added 5 to 6 drops of concentrated hydrochloric acid, then magnesium ribbon and observed for pink or red coloration [22, 23].

TANNINS

Dissolved 20 mg of extracts or fraction in 1.5 ml of distil water and added 2-3 drops of ferric chloride solution, appearance of blue or green black coloration indicate presence of tannins [22, 23].

SAPONINS

Added 30 mg of the plant extracts into 10 ml of distilled water and shake well, the appearance of froth persistence indicate saponins [22, 23].

PATHOGENIC BACTERIAL CULTURES

Escherichia coli (ATCC, MDR), *Pseudomonas aeruginosa* (ATCC, MDR), *Salmonella sp, Staphylococcus aureus* (MRSA) and *Shigella sp* were obtained from the Department of Microbiology, Kohat university of science and technology. All the test strains were maintained in nutrient broth and were sub-cultured for every

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two-week. These bacteria were the test pathogens for the current antibacterial assay.

ANTIBACTERIAL ACTIVITY ASSAY

Antibacterial Activity of *n*-hexane, chloroform, ethyl acetate and water soluble extracts of each plant was determined by Ager well diffusion method described by M. Arifullah et al. with some modifications [24]. Muller-Hinton agar (MHA) was used as the growth media and was prepared by dissolving 38g of MHA per liter of distilled water. After preparing the media (MHA), it was autoclaved, cooled up to 45˚C, poured into Petri plates and made five wells with the help of cork borer of 6mm diameter, four wells for the four different extracts and one for the negative control (DMSO). The stock solutions of four extracts of each plant with the concentration of 20mg per ml were prepared in DMSO. Ceftazidime standard disc (30µg) was used as a positive control against each bacterial strain for comparative efficacy. Inoculation of the bacterial strains on media, filling of wells with extracts and negative control was performed in laminar flow cabinet so as to avoid contamination. Then the plates were incubated for at 37°C for 24 hours and zone of inhibition around the wells if any was measured in mm (millimeter).

RESULTS

PHYTOCHEMICAL SCREENING OF THE PLANTS

The four different fractions of the methanolic extract of each plant were analyzed qualitatively and find the following phytochemicals which are given in the following tables 1, 2 and 3.

TABLE 1: QUALITATIVE PHYTOCHEMICAL ANALYSIS OF *INULA CRITHMOIDES*

Plant fractions	Alkaloids	Flavonoides	Saponins	Tannins
n-Hexane	+	_	+	_
Chloroform	+	+	_	_
Ethyl acetate	+	+	_	_

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Aqueous	+	+	+	+

Key: +: Present –: Absent

TABLE 2: QUALITATIVE PHYTOCHEMICAL ANALYSIS OF *ASTRAGALUS ADSCENDENS*

Plant fractions	Alkaloids	Flavonoides	Saponins	Tannins
n-Hexane	+	_	+	_
Chloroform	+	_	+	_
Ethyl acetate	+	+	_	_
Aqueous	+	+	+	_

Key: +: Present –: Absent

TABLE: 3. QUALITATIVE PHYTOCHEMICAL ANALYSIS OF *HELIOTROPIUM EICHWALDII*

Plant fractions	Alkaloids	Flavonoides	Saponins	Tannins
n-Hexane	+	+	_	_
Chloroform	+	_	_	+
Ethyl acetate	+	_	+	+
Aqueous	+	+	+	+

Key: +: Present –: Absent

ANTIBACTERIAL ACTIVITY

Four different fractions of methanolic extract of each plant were subjected to antibacterial activities against the selected bacterial strains namely *Escerichia coli* (ATCC, MDR), *Psedumonas aurigenosa* (ATTC, MDR), *Salmonella sp*, *Methicillin-resistant Staphylococcus aureus* (MRSA) and *Shegilla sp* that contribute in diarrhoeal and urinary tract infections. Dimethyle sulphoxide was used as a negative control so as to check the purity of the solvent. The DMSO did not show any activity and proved the purity of the solvent. Ceftazidime (CAZ) was used as the positive control against all the bacterial strains. It was active against all the

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bacterial strains. Fractions of each plant showed different inhibition zone at 20 mg/ml concentration. The results have been given in the table no 4, 5, and 6.

Bacterial Strains	*n*-Hexane (mm)	Chloroform (mm)	E.Acetate (mm)	Aqueous (mm)	Ceftazidime (mm)	DMSO (mm)
E.coli (ATCC)	12.16±0.18	12.2±0.21	13.13±0.24	11.33±0.23	14	0
E.coli (MDR)	0	0	10.3±0.21	9.1±0.26	12	0
P.aeruginosa (ATCC)	11.06±0.30	12.23±0.32	12.23±0.32	8.1±0.26	14	0
P.aeruginosa (MDR)	0	07.1±0.26	10.2±0.16	11.1±0.29	12	0
Salmonella sp	14.03±0.36	08.1±0.26	14.1±0.29	12.16±0.18	30	0
Shegilla sp	13.4±0.16	12.16±0.18	11.16±0.23	13.4±0.16	18	0
MRSA	0	12.33±0.12	12.13±0.26	12.33±0.12	20	0

TABLE: 4. ANTIBACTERIAL ACTIVITY OF DIFFERENT FRACTIONS OF THE METHANOLIC EXTRACT OF *INULA CHRITHMOIDES* AGAINST SELECTED PATHOGENS

±Standard deviation , Ceftazidime = +ve control, Dimethyl sulfoxide (DMSO) = -ve control

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Vol. 2 , Issue. 4 (2024)

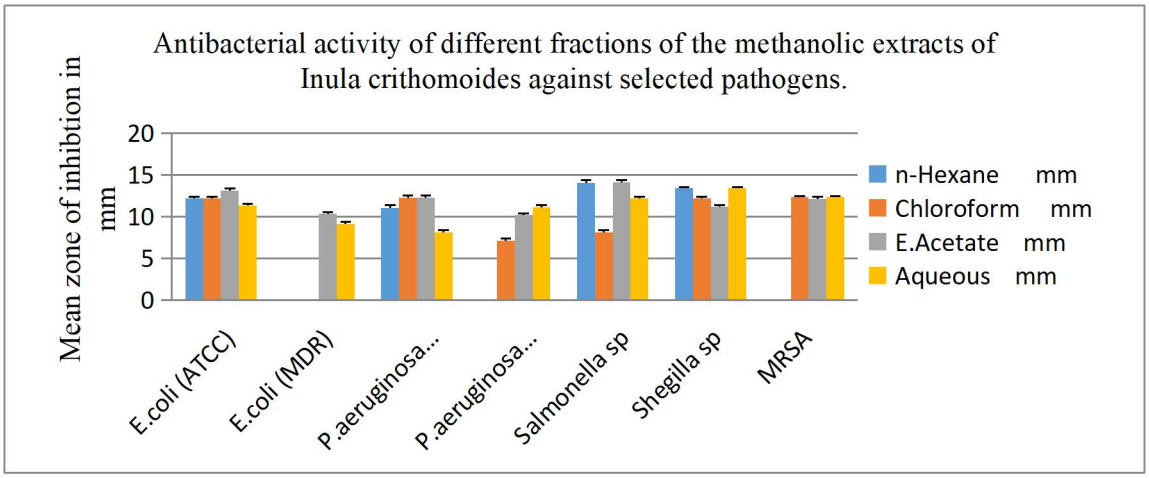

Figure: 1. Inhibition zone of four different fractions of the methanolic extract of the plant. Each column represents mean value of three independent replicates and the error bars indicate standard deviations.

TABLE 5: ANTIBACTERIAL ACTIVITY OF DIFFERENT FRACTIONS OF THE METHANOLIC EXTRACT OF *ASTRAGALUS ADSCENDENS* AGAINST SELECTED PATHOGENS

Bacterial Strains	*n*-Hexane (mm)	Chloroform (mm)	E.Acetate (mm)	Aqueous (mm)	Ceftazidime (mm)	DMSO (mm)
E.coli (ATCC)	0	11.26±0.20	12.03±0.12	13.23±0.20	14	0
E.coli (MDR)	0	10.06±0.24	08.13±0.26	08.16±0.23	12	0
P.aeruginosa (ATCC)	08.13±0.26	0	07.1±0.14	10.26±0.20	14	0

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Name of Publisher: DIVINE KNOWLEDGE INSTITUTE
Vol. 2 , Issue. 4 (2024)

P.aeruginosa (MDR)	0	0	0	08.13±0.26	12	0
Shegilla sp	12.03±0.12	12.16±0.23	13.1±0.29	12.03±0.12	18	0
Salmonella sp	12.06±0.18	10.23±0.20	12.03±0.12	11.13±0.26	30	0
MRSA	12.03±0.20	10.16±0.18	12.03±0.20	11.13±0.26	20	0

±Standard deviation , Ceftazidime = +ve control, Dimethyl sulfoxide (DMSO) = -ve control

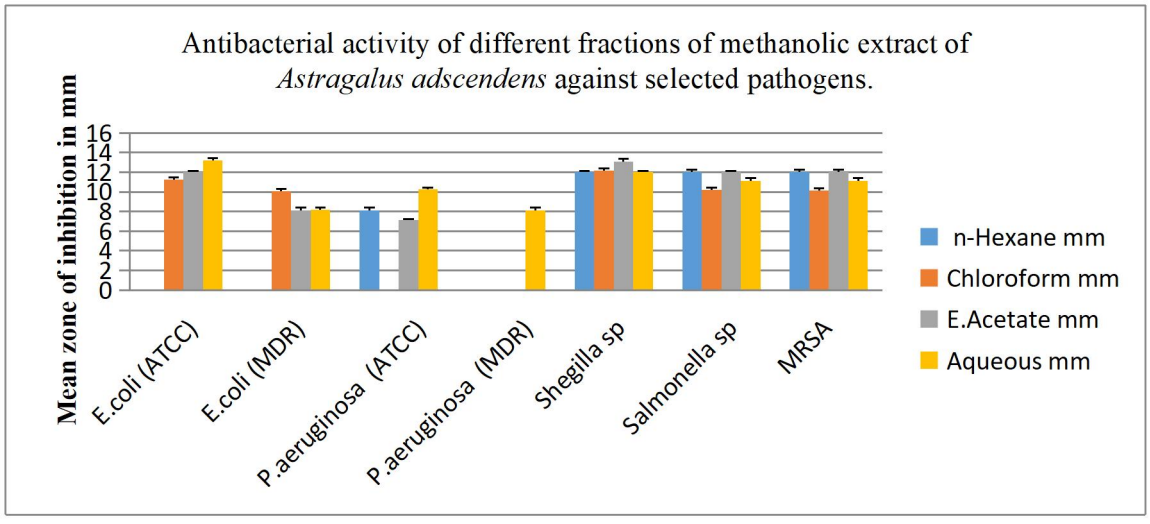

Figure: 2. Inhibition zone of four different fractions of the methanolic extract of the plant.The mean value of three independent replicates is shown in each column, and standard deviations are shown by the error bars.

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Print ISSN 3006-9335
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Name of Publisher: DIVINE KNOWLEDGE INSTITUTE
Vol. 2 , Issue. 4 (2024)

TABLE 6: ANTIBACTERIAL ACTIVITY OF DIFFERENT FRACTIONS OF THE METHANOLIC EXTRACT OF *HELIOTROPIUM EICHWALDII* AGAINST SELECTED PATHOGENS

Bacterial Strains	*n*-Hexane (mm)	Chloroform (mm)	E.Acetate (mm)	Aqueous (mm)	Ceftazidime (mm)	DMSO (mm)
E.coli(ATCC)	14.03±0.20	12.16±0.23	08.36±0.12	14.03±0.20	14	0
E.coli (MDR)	09.23±0.24	08.1±0.14	0	10.26±0.20	12	0
P.aeruginosa (ATCC)	09.23±0.24	10.26±0.20	10.26±0.20	10.1±0.14	14	0
P.aeruginosa (MDR)	12.2±0.16	08.1±0.14	09.23±0.24	12.26±0.20	12	0
Shegilla sp	13.26±0.20	12.16±0.23	10.1±0.14	13.26±0.20	18	0
Salmonella sp	15.2±0.24	18.3±0.12	10.23±0.20	12.2±0.16	30	0
MRSA	10.1±0.14	10.26±0.20	10.2±0.16	12.2±0.16	20	0

±Standard deviation , Ceftazidime = +ve control, Dimethyl sulfoxide (DMSO) = -ve control

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Vol. 2 , Issue. 4 (2024)

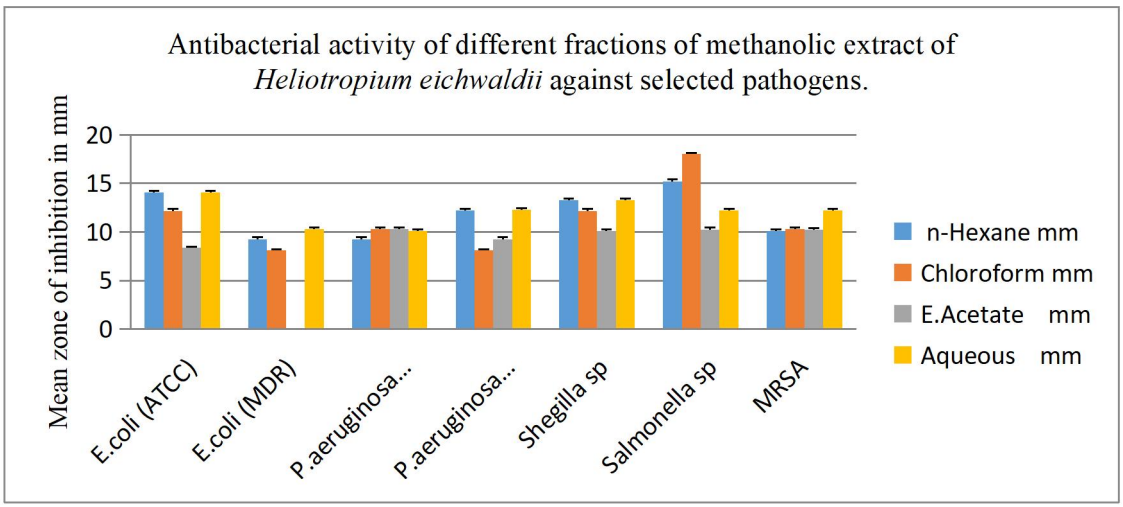

Figure: 3. Inhibition zone of four different fractions of the methanolic extract of the plant. The mean value of three independent replicates is shown in each column, and standard deviations are shown by the error bars.

DISCUSSION

Plants are considered to be the most accessible and promising source of new therapeutically active chemicals that can be helpful in drug development. Different parts of these plants like their roots, bark, flowers, seeds and leaves etc. may used by the people selectively or in combination with each other. According to estimation by WHO, approximately more than 80% of the total people of the poor countries depend upon the conventional drugs [25]. The medicinal importance of the plants is due to their chemical constituents called phytochemicals which interact with human physiology and exert valuable effects [26]. Particularly the secondary metabolites are responsible for medicinal value of plants. The metabolites such as alkaloids, flavonoids, tannins, terpenes and phenolic compounds are therapeutically important [27]. For this reason first of all, phytochemicals such as alkaloids, saponins, flavonoids and tannins were analyzed. Recently studies have shown that these phytocontituents have medicinal values [28]. Phytochemical analysis of *I. crithmoides* given in table (1) show that alkaloids

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Vol. 2 , Issue. 4 (2024)

are present in its all the fractions, flavonoides are also present in all the fractions except n-hexane, saponins are present only in the n-hexane and aqueous fraction while tannins are found only in the aqueous fraction. These results determine the richness of alkaloids and flavonoides in *I. crithmoides*. Similarly table (2) show that all the fractions of *A. adscendens* contain alkaloids, flavonoides are present only in ethyl acetate and aqueous fraction, saponins are present in all the fractions except ethyl acetate while all the fractions showed the absence of tannins. These results determine the richness of alkaloids and saponins in *A. adscendens*. The phytochemical screening of *H.eichwaldii* given in table (3) also shows the presence of alkaloids in its all the fractions, flavonoides are present only in the n-hexane and aqueous fractions, saponins are present only in ethyl acetate and aqueous fractions while tannins are present in all the fractions except in n-hexane fraction. These results show the richness of alkaloids and tannins in this plant.

EVALUATION AGAINST DIARRHEAL AND URINARY TRACT INFECTIOUS BACTERIAL PATHOGENS

Plants are considered the key source of therapeutically active agents and drugs development. Antibacterial evaluation of the plants is the primary step to achieve this goal [29]. The antibacterial activities of the 4 different fractions of the methanolic extract were evaluated by the inhibition zone around the well. For the explanation of antibacterial assay results, we used the following scale of measurement; zone of inhibition of equal to 15 or >15mm as strongly inhibitory, 10-14mm as moderately and <10mm as weakly inhibitory. Table (4) shows that most of the fractions of *I. crithmoides* are active against the selected pathogens but most of the zones of inhibitions are in moderately and weakly inhibitory range. So this plant can be considered as moderately active against the selected pathogens. The inhibitory potential of moderately range has been shown by essential oils of *I. crithmoides* against *Staphylococcus aureus* (ATCC 27853) [30]. Similarly inhibitions shown by most of the fractions of *A. adscendens* given in table (5) are in

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Print ISSN 3006-9335
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Name of Publisher: DIVINE KNOWLEDGE INSTITUTE
Vol. 2 , Issue. 4 (2024)

moderately range while few have shown no activity. Overall this plant can also be considered as moderately active. The zones of inhibition of *H.eichwaldii* given in table (6) are also mostly in the moderately range except the n-hexane and chloroform fraction which have shown strong inhibition against *salmonella* specie. An unexpected result has been shown by the n-hexane fraction against *P. aeruginosa* species, it was found to be strongly inhibitory against *P. aeruginosa* (MDR) rather than *P. aeruginosa* (ATTC). Overall this plant can also be considered moderately active.

CONCLUSIONS

The results of the current studies clearly showed the existence of important phytochemicals such as alkaloids, saponins, flavonoids, tannins etc. in these plants and most of the fractions of each plant have antibacterial potential against the selected diarrhoeal and urinary tract infectious pathogens except few of which showed no activity. So it has been concluded from the current study that these plants might be exploited as natural drugs for the treatment of diarrhoeal and urinary tract infections caused by bacteria.

Author Contributions: A.K. (Abdul Khaliq) and W.U. (Wasim Ullah) conceived the idea and designed the experiments; A.K. and W.U. performed the experiments; A.K., W.U., I.U.K. (Ismat Ullah Khan) and A.S., (Abdul Shahab) analyzed the data; A.K. and W.U., wrote the paper; A.K., W.U and A.S. did proof reading; A.K., W.U. and I.U.K., critically evaluated and reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

Acknowledgments: The author is thankful to Kohat University of Science and Technology Kohat, Pakistan for providing research facilities and vibrant research environment.

Conflicts of Interest: The authors declare no conflict of interest

The Cancer Research Review
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Print ISSN 3006-9335
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Vol. 2 , Issue. 4 (2024)

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The Cancer Research Review
Online ISSN 3006-9343
Print ISSN 3006-9335
THE CANCER RESEARCH REVIEW
Online ISSN 3006-9343
Print ISSN 3006-9335
http://the-crr.com/index.php/Journal
Name of Publisher: DIVINE KNOWLEDGE INSTITUTE
Vol. 2 , Issue. 4 (2024)

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