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EDITORIAL

Life Science Journal of Pakistan
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Editorial – Issue 1, Volume 5

LSJP is going to publish its sixth issue and entering 5th year of publishing. LSJP is gaining popularity among life science researchers who are sending their valuable articles for publication across all over Pakistan. We have currently introduced one new feature to LSJP website, the *Just In* feature enables the articles to appear on-line as soon as they are accepted. Team LSJP congratulates Prof Dr Imran Amin (Editor Plant Biotechnology, LSJP) for his meritorious achievement on receiving Gold Medal from Pakistan Academy of Sciences, in the field of Emerging Sciences and Biotechnology.

In current issue, four manuscripts have been selected for publication, out of which three are original research articles and one mini-review article. First manuscript focusing on prevalence and aetiology of hydronephrosis in adults attending one of the radiological and medical imaging departments. Authors reported that around half (45%) of investigated middle aged persons had higher prevalence of hydronephrosis among them 30% females and 70% were males. About 86% had hydronephrosis in unilateral kidney and 13% in bilateral kidneys with highest in Grade 2 in over 57.3% subjects. They concluded ultrasonography as useful tool in identifying hydronephrosis and determining its aetiological factors, further, renal calculi are the most prevalent cause of hydronephrosis followed pregnancy and benign prostatic hypertrophy. Second original research accepted reported descriptive cross-sectional study depicting prevalence of HIV and its associated factors among prisoners of one prison. Although the prevalence HIV was 1 %, however prisoners are at higher risk of experiencing HIV, as over one third (36.7%) were drug users, 8.6% used an injectable form of drug, while 84.3% never used condoms during the sex. Prisoners are at high risk of experiencing HIV due to drug addiction, intravenous drug usage, sharing of syringes and razors as well as unsafe sexual practices. Authors suggested recommended health awareness sessions for prisoners to keep them safe from HIV/AIDS. Third manuscript accepted for publication was also of great importance reporting phytochemical analysis and antidiabetic activity of common medicinal herbs *Withania somnifera* and *Cnidium monnieri* using animal models. Authors report significant decrease in body weight leading a decrease in insulin level and also had cytotoxic effect closer to normal value. Presence of different phytochemicals, flavonoids, glycosides, steroids, and triterpenoids phenolic compounds, flavonoids and antioxidants in reported herbs offer evidence to promote the restoration of alloxan-induced diabetic harm in rats. They concluded that impaired glucose tolerance and insulin resistance appeared as an efficient means of regulating glucose levels.

A mini-review focusing prospects of using nanotechnology for the treating HCV was also included in this issue. That review describes that available treatment for HCV develops a lot of side effects therefore nanotechnology based solutions are becoming popular due to small amount consumed for treatment in the form of Nanoparticles, bio-conjugation, micelle development and dendrites. Instead of utilizing ribavirin alone, acylated polyglycerol adipate (PGA) NPs and polyglycerol adipate (PGA) NPs may be used to transfer perturbating hydrophobicity of ribavirin and increases the capacity of the NPs to assemble pharmaceuticals. Furthermore, nanoparticle may cross the blood–brain barrier (BBB) comparatively easily for therapeutic handling of neurological conditions. This review summarized role of nanoparticles (NPs) as vehicle for anti-HCV vaccination, anti-HCV DNA enzymes, anti-HCV adjuvants, and anti-HCV phenolic chemicals and their targeted administration.

Team LSJP made every effort to make the process of manuscript submission, review and publication convenient and easy. Efforts of LSJP team are highly acknowledged for their help and support to bring LSJP at this level of gaining excellence in life sciences publications. LSJP will continue addressing scientific trends related to all disciplines mentioned in the scope of this journal, for that we hope more and active participation of scholars from academia and R&D institutes.

Dr. Yasar Saleem,

Managing Editor,

Life Science Journal of Pakistan

ORIGINAL RESEARCH

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Prevalence and Aetiology of Hydronephrosis in adults

Akash John[1], Tallat Anwar Faridi[2], Ali Junaid Dar[3], Syed Bilal Hassan[4], Iqra Hamid[5], Kubra Samreen [6]

1. University Institute of Radiological and Medical Imaging Sciences, The University of Lahore, Gujrat Campus
2. University Institute of Public Health, The University of Lahore (UOL), Lahore
3. University Institute of Radiological and Medical Imaging Sciences, The University of Lahore, Gujrat Campus
4. University Institute of Public Health, The University of Lahore (UOL), Lahore
5. University Institute of Public Health, The University of Lahore (UOL), Lahore
6. Sharif Medical City Hospital, Lahore

***Corresponding Author**
Akash John
University Institute of Radiological Sciences and Medical Imaging, University of Lahore, Gujrat Campus
Email: akashjohn10048@gmail.com

ABSTRACT

Introduction: Hydronephrosis is usually caused by an underlying medical condition or risk occasionally as congenital blockage, unilateral obstructive uropathy, kidney stones, UTIs, tissue scarring, blood clots, neuromuscular problems, Cancer or BPH and pregnancy. This current study was directed to determine the etiological factors and prevalence causes of Hydronephrosis

Material and Methods: A Retrospective study was conducted at two private health care setups in Gujranwala, Pakistan. After Informed consent data was collected over period of 8 Months Jan 2020 to Sep 2020. Data was analysed on SPSS version 20 frequencies and percentages were mentioned. Aetiological factors of Hydronephrosis were evaluated on ultrasound.

Results: This study included 213 patients, with those aged 41-50 years (45%) having the highest prevalence of hydronephrosis. Gender Includes 30% females and 70% males. About 86% had Hydronephrosis in Unilateral kidney and 13% in bilateral kidneys. The grading of Hydronephrosis was found as highest in Grade2: 122 (57.3%). The causes of Hydronephrosis were observed on Ultrasound and found most prevalent cases of Calculi 60%, 13% females had Hydronephrosis due to Pregnancy, 8.9% males had Hydronephrosis due to Benign Prostatic Hyperplasia.

Conclusion: The study concluded that Renal Calculi are the most prevalent cause of Hydronephrosis followed Pregnancy and BPH.

Keywords: Hydronephrosis, Aetiology, Renal Calculi, BPH, Pregnancy

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INTRODUCTION

Hydronephrosis occurs when an obstruction stops the urine from kidneys to drain into the bladder[(1)]. The obstruction can cause swelling of kidneys which can be unilateral or bilateral[(2)]. The kidneys filter the blood and eliminate extra waste materials from the body[(3)]. The fluid gets accumulated in the renal pelvis and get transferred to urinary bladder via narrow tubular structures called as ureters which have narrow constrictions and may be the common site for obstruction by calculi[(4)]. Hydronephrosis usually happens when passage of urine is obstructed or the reflux when urine reverse back causing the renal pelvis to swell[(5)]. Obstruction causes an increase in urinary tract stress leading to biochemical and morphological alterations[(6)]. The kidney's regular function necessitates the elimination of final metabolic products as well as an excessive amount of water[(7)]. The urinary outflow can be restricted or there can be retrograde migration of urine which remains in the bladder can lead towards enlarged renal pelvis[(8)] [(9)]. Despite medical advances, Hydronephrosis remains a major issue[(10)]. The urologists face a lot of problems due to partial or total obstruction which is a common health problem[(1, 11)].

Hydronephrosis is usually caused by an underlying medical condition or risk occasionally as congenital blockage, unilateral obstructive uropathy, kidney stones, UTIs, tissue scarring, blood clots, neuromuscular problems, Cancer or

BPH and pregnancy.[11, 12] According to modern research Hydronephrosis (or hydroureter) is the most frequent condition, although ureteral and renal pelvic dilatation is more apparent on the right side of the body and occurs in 80 to 90% of pregnant women.[13, 14] Using ultrasonography, maternal Hydronephrosis is most commonly found during the beginning of the third trimester,[15, 16] which experts believe is owing to progesterone's actions on the ureters, which lower their tone.[17] The specific origin and presentation of Hydronephrosis or hydroureter in adults vary from neonates and children. [18] The most frequent birth abnormalities that induce Hydronephrosis in foetuses and new-borns are ureter pelvic junction blockage and vesico-ureteral reflex.[19, 20] Major cause of bladder outlet obstruction in young individuals is kidney stone which can be single and multiple, followed by tumours, neurogenic bladder, and inflammatory ureteral strictures.[14] While in older patients Renal Calculi, benign prostatic hyperplasia or carcinoma in men, pelvic neoplasm can be the most common causes for Hydronephrosis.[21, 22]

Hydronephrosis sometimes may or may not be Symptomatic.[23] A pain and discomfort on back and the side of abdomen or groin area known as Flank pain is common symptom.[24] Some other signs and symptoms include nausea, fever, pain while urination, frequency, urgency, incontinence and incomplete urination.[25] The severity of the disease vary in showing signs and symptoms.[21] The most common sign for Hydronephrosis is flank pain in contrast to the other disorders like Inflammation in Urinary tract, chronic and acute kidney failure.[26] The society of foetal urology (SFU) classification scheme divides the Hydronephrosis into five groups as Grade 0 to 4.[27] Hydronephrosis is not present in grade 0 patients. Patients of Grade 1 can have Mild Dilatation of the renal pelvis. Patients of Grade 2 can have mild dilatation of the renal pelvis along with dilatation of major calyces. Patients of Grade 3 have moderate dilations involving all calyces. Patients in Grade 4 have severe dilations along with dilatation of all calyces and thinning of the renal parenchyma[28] .

Radiological imaging like ultrasound can reveal the importance of urodynamic and the existence of Hydronephrosis[29]. To avoid difficulties, clear parameters and hazardous findings that are symptomatic of renal injury must be diagnosed as soon as possible. This research will aid in the diagnosis and treatment of mild Hydronephrosis before it progresses to acute and chronic renal failure.

MATERIALS AND METHODS

It is a Retrospective study conducted at two private health care setups in Gujranwala, Pakistan. After Informed consent data was collected over period of 8 Months from January 2020 to September 2020. Following the study period, all patients identified with Hydronephrosis during an ultrasound scan investigation presented at the study location were enrolled. Data was collected using convenient approach on specially designs sheet in which age, gender, Unilateral Kidney or Bilateral Kidneys and its Grading of Hydronephrosis were recorded. Data was analysed on SPSS version 20. The causes were confirmed by considering history, lab reports and ultrasound evaluation on Toshiba SSA-770A, 3.5 MHz with convex transducer was used to evaluate patients.

RESULTS

Patients presenting to the radiology department for ultrasound scanning were evaluated in the current study, and the aetiology of hydronephrosis was discovered. In Table 1 age distribution of patients with Hydronephrosis is written, in which the most Prevalent age group of 41-50 years 96 (45%) patients presented with Hydronephrosis. The female patients in this inclusion were 64 (30%) and 149 (70%) were males. The kidney involvement in terms of sides is shown as 185 (86%) hydronephrosis due to disease in the unilateral kidney and 28 (13%) involvement in both or bilateral kidneys. In Table 1 the grading of Hydronephrosis was mentioned as Grade 1: 33 (15.5%), Grade 2: 122 (57.3%), Grade 3: 39(18.3%), Grade 4: 19(8.9%). The causes of Hydronephrosis was observed on Ultrasound Equipment and results shows that most Prevalent cases of Calculi 129 (60%) causing Hydronephrosis, 28 (13%) females had Hydronephrosis due to Pregnancy, 19 (8.9%) males had Benign Prostatic Hyperplasia and 6 (2.8%) had Prostate cancer. About 4 Patients (1.9%) had PUJ stenosis causing Hydronephrosis. About 27 Patients (12.7%) the finding of cause of Hydronephrosis was undetermined.

DISCUSSION

In current study the diagnosis of Hydronephrosis was evaluated on Ultrasound in which the grading of Hydronephrosis was mentioned. SFU grading such as Patients of Grade 1 can have Mild Dilatation of the renal pelvis. Patients of Grade 2 can have mild dilatation of the renal pelvis along dilatation of major calyces. Patients of Grade 3 have moderate dilations along dilatation of all calyces. Patients of Grade 4 have severe dilations along dilatation of all calyces and thinning of the renal parenchyma.

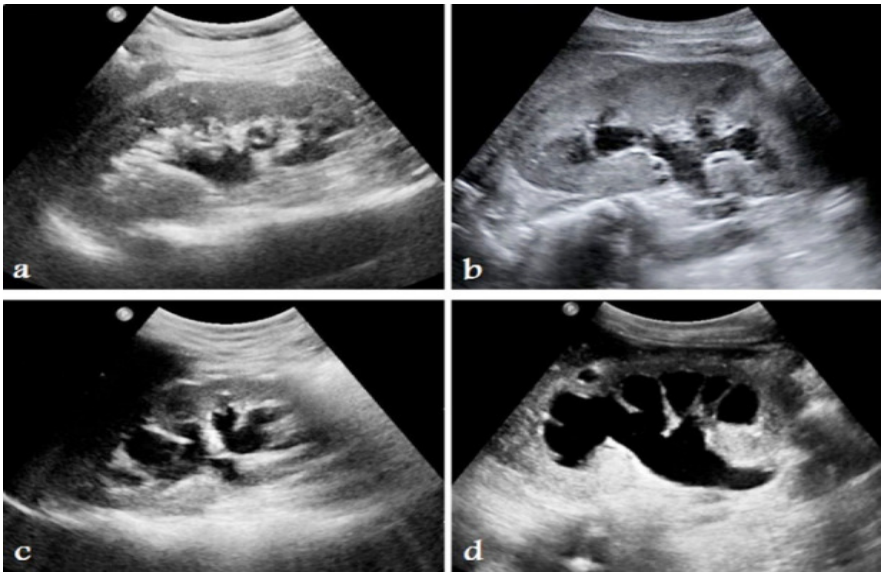

Figure 01: Right kidney of patients showing Grade1 (a), Grade2 (b), Grade3 (c), Grade4 (d) Hydronephrosis according to SFU grading system[27]

Table 01: Showing the frequency and percentages of age groups, Gender, Involved Kidney/s, and Aetiology of Patients having Hydronephrosis

Variables	Categories	Frequency	Percentage
Age Groups	20-30	46	21.6
	31-40	71	33.3
	41-50	96	45.1
	Total	213	100.0
Gender	Female	64	30.0
	Male	149	70.0
	Total	213	100.0
Kidney/s	Unilateral Kidney	185	86.9
	Bilateral Kidneys	28	13.1
	Total	213	100.0
Grading of Hydronephrosis	Grade 1	33	15.5
	Grade 2	122	57.3
	Grade 3	39	18.3
	Grade 4	19	8.9
	Total	213	100.0
Aetilogy of Hydronephrosis	Calculi	129	60.6
	Pregnancy	28	13.1
	BPH	19	8.9
	Prostate Cancer	6	2.8
	PUJ Stenosis	4	1.9
	Not Determined	27	12.7
	Total	213	100.0

In 1993, S. K. Fernbach published a study and explained that SFU has tried to standardise ultrasonography performance and grading systems. At that time SFU members created and used an ultrasound-based approach to grade Hydronephrosis in 36 institutions. The current study has graded as Grade 1: 33 (15.5%), Grade 2: 122 (57.3%), Grade 3: 39(18.3%), and Grade 4: 19 (8.9%). The presence of the calices, renal pelvis and renal parenchyma are major constituents for the use of the grading for Hydronephrosis.

A retrospective study by Sultan Abdul Waddod Published in 2021 in Pakistan explains the Hydronephrosis by examining 233 patients which included 91.41% were adults following 66.10% as male and 33.90% as female. The current study also has the similar findings of Hydronephrosis in which most common age group of 41-50 years was 45%. The patients included in this study were 30% females and 70% males relating with the previous literature article mentioned. About (57.3%) in Grade 2 Hydronephrosis was evaluated in current study whereas it had almost similar result relating as 58% of patients suffering from grade-2, 21.5% in grade-3, 11.6% in grade-1, and 8.2% grade-4 in previous research. He also found the causes as 54.1% as Calculi in terms of cause of Hydronephrosis. The etiological findings of current study found that most Prevalent cases of Calculi were 60% causing Hydronephrosis, 13% due to Pregnancy, 8.9% males had Benign Prostatic Hyperplasia and 2.8% had Prostate cancer. About 1.9% had PUJ stenosis causing Hydronephrosis. About 12.7% of the findings on ultrasound were undetermined.

Another study by Gowadhan Dare published in 2019 and goal of his study was to look at the causes, symptoms, diagnostic methods, and treatment possibilities for unilateral Hydronephrosis. He conducted a study in a tertiary care Hospital in which he examined and evaluated 72 unilateral Patients on ultrasound and found that 50 (69.44%) of Hydronephrosis were due to ureteric calculi, PUJ obstruction 18 (25%) and renal calculi 4 (5.56%). He has similar results with current study in which the kidney involvement was 185 (86%) in Unilateral kidney and 28 (13%) as Bilateral kidneys. In current study the causes of Hydronephrosis were observed on Ultrasound Equipment as prevalent cases of Calculi were 129 (60%) causing Hydronephrosis, 28 (13%) females had Hydronephrosis due to Pregnancy, 19 (8.9%) males had Benign Prostatic Hyperplasia and 6 (2.8%) had Prostate cancer. About 4 Patients (1.9%) had PUJ stenosis causing Hydronephrosis which is almost similar to the previous study. He came to the conclusion that ureteric calculus, renal calculus and obstruction at pelvic-ureteric junction were the aetiological reasons for unilateral Hydronephrosis and that treatment should be tailored to the aetiology.

CONCLUSION

In conclusion ultrasonography is helpful in identifying Hydronephrosis and determining its aetiological factors. Ureteral and kidney stones are the most prevalent cause of Hydronephrosis. Pregnancy was the second most prevalent cause of Hydronephrosis in women, while benign prostatic hypertrophy was the third most prevalent cause in men.

CONFLICTS OF INTEREST

There was no conflict of interests between authors.

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There was no funding source.

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ORIGINAL RESEARCH

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The Prevalence of HIV and its Associated Factors among Prisoners of Central Prison, Larkana, Pakistan

Kaleem Abro[1], Mudasir Mushtaq[2], Tariq Feroz Memon[3], Saeed Ahmed Shaikh[1], Muhammad Ibrahim[4], Sheeraz Hyder Khokhar[5], Sajida Perveen[6], Salma Memon[7], Munawar Hussain Soomro[1]

1- Chandka Medical College, Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU) Larkana, Pakistan
2- Health Services Academy, Islamabad, Pakistan
3- Department of Community Medicine, Liaquat University of Medical & Health Sciences, Jamshoro, Pakistan
4- Bibi Asifa College of Nursing, SMBBMU, Larkana, Pakistan
5- Health Department Sindh, Larkana, Pakistan
6- National Institute of Psychology, Quaid-i-Azam University, Islamabad, Pakistan
7- Sindh Education Department, Hyderabad, Pakistan

Corresponding author:
Dr. Munawar Hussain Soomro
Department of Community Medicine and Public Health, Chandka Medical College, Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU) Larkana, Pakistan.
Email address: munawar_soomro@hotmail.com
Contact number: +92 334 507 48 44

ABSTRACT

Introduction: HIV/AIDS is one of the major worldwide health problems affecting inmates and a significant concern for government, public health services and prison administration services. The aim of our study was to determine the prevalence of HIV infection among prisoners and its associated factors.

Material and Methods: A descriptive cross-sectional study was carried out among prisoners of Central Prison, Larkana, Pakistan from August 2019 to December 2019. A total number of Seven hundred and eighty-three (N = 783) prisoners were invited to participate. Data were collected by means of the pre-designed and pilot tested study questionnaire and were entered in SPSS version 21 for analysis.

Results: Out of 783 participants initially invited to the study, six hundred (N = 600) of whom fulfilled the criteria. The screening and questionnaire response rate was 81%. During screening three prisoners were found to be HIV positive. Among prisoners, 220 (36.7%) were drug users, 19 (8.6%) used an injectable form of drug, while 506 (84.3%) had never used condoms during the sex. The prevalence of this study was 1.00%

Conclusion: The study revealed the need to educate prisoners for prevention and care measures in prisons. Further studies are needed to observe the situation in other part of the country.

Keywords: HIV, Acquired Immunodeficiency Syndrome (AIDS), Prevalence, Prisoners, Larkana

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INTRODUCTION

Human Immunodeficiency Virus (HIV) or acquired immunodeficiency syndrome (AIDS) is a major public health issue among prisoners in many countries. It is one of the serious challenges for governments, public health services, and prison administration services. and has become a main global challenge. It has quickly affected millions of people irrespective of age and gender throughout the globe (1). The causative agent for AIDS is HIV and its major associated risk factors are unsafe sex, sharing of injectable equipment and infected blood transfusion (2). The AIDS weakens the immune system of the human body; consequently, the body becomes non-resistant to various diseases. As a result, disturbed mental health, compromised social life, as well as high morbidity and mortality take place (2, 3). Studies have reported that, there are more inmates who are HIV-positive than people in the general population (4-7). According to the Joint United Nations Programme on HIV/AIDS (UNAIDS) globally 38 million people were infected with HIV in 2019, with 22 million of them were under treatment (1). Meanwhile, in Pakistan, 1.9 million people were infected with HIV in 2019 (8). Among the most vulnerable groups to HIV infection are the youth of the age group 15-24 years and half of all new infections are caused globally in this age group every year (9, 10). Annually, the incidence of HIV is approximately two million cases throughout the world (1).

Most of these cases are reported to have spread through saliva, sperm or breast milk (11). After getting entry into the human body, HIV being a lentivirus, also known as "weak virus", stays in the body for a long period. Simultaneously, it keeps on dividing and entering data into host cell's DNA. While in the human body, it infects cells of the immune system, such as CD4+ cells, macrophages and dendritic cells. CD4+ cells play a vital role in immune system maintenance, however once they are attacked by HIV virus, their rapid decline in skin and immune system occurs. Consequently, HIV infection turns into AIDS in the human body (12). The outbreak of HIV in Ratodero town, district Larkana, Sindh province in 2019 caught focus of health agencies throughout the world. The World Health Organisation (WHO) declared it as Grade-2 Health Emergency (13).

Prisons are among the most restricted and marginalized populations to access the health services, interventions, and surveys. Whereas they are an endangered population for acquiring infectious diseases particularly the HIV, due to the people from various backgrounds, communities and risk factors are kept together for varying period of time. According to the ministry of law, justice and human rights of Pakistan; the total number of prison facilities in the country are ninety-eight (98), and with a total number of 77,275 prisoners (14) Whereas twenty-four prison facilities are in the province of Sindh. Hence, this study has been carried out in Central Prison of district Larkana, Sindh Prisoners were chosen as the study population because they are a venerable group and are prone to communicable infections like HIV. This study will therefore add on valuable current data regarding prevalence of HIV in this vulnerable population. Identification of HIV cases among prison inmates will sensitize all concerned stakeholders to focus further on the increasing pool of HIV cases among prison inmates and will be helpful in designing new programs and policies to improve health of these prisoners.

The objective of the study therefore was to assess the prevalence of HIV infection among prisoners and its associated factors in Central Prison of Larkana.

METHODS

A descriptive cross-sectional study was conducted in the central prison of District Larkana, in Sindh province, Pakistan (Figure 1) from August 2019 to December 2019. The study population was male prisoners of the central prison, as the prison confined only male prisoners. Every prisoner was informed about the importance of the study. All prisoners of the central prison of Larkana available at the time of study and willing to participate in the study; including those prisoners who had already been diagnosed as HIV positive were included in the study. Seven hundred and eighty-three (783) prisoners were invited to participate. Prisoners who had already been screened in the last two months and found negative, prisoners not willing to participate in the study and the prisoners who seemed incapable of understanding the information about the survey due to intoxication, drug withdrawal or cognitive impairment were excluded from the study. After checking eligibility, a total number of six hundred (600) prisoners were included in the study. After reaching the jail dispensary with the permission of the superintendent central jail, the principal investigator along with three research assistants went to every barrack for conducting health awareness sessions regarding HIV/AIDS and obtaining verbal informed consent for the study from prisoners. The study participants were asked questions from a pre-designed questionnaire, which was developed through the help of literature as per guidelines of the World Health Organization (WHO) regarding risk factor assessment of HIV (15). The pre-designed questionnaire was pilot tested and revised before the final data collection. The identity of the study participants was kept confidential by excluding identity details in the questionnaire.

The blood technician/paramedic of the study team drew 2cc of the blood sample by using a 3ml auto-disposable syringe from each participant. The blood was preserved in yellow tubes that were brought to the Central Pathology Laboratory, Chandka Medical College, Larkana for testing purposes with due permission from Medical Superintendent, Chandka Medical College Hospital, Larkana. After centrifuging the blood, the serum was tested on WHO approved SD HIV ½ 3.0 Bio Line kit for screening (16). Ethical approval of the study was taken from the Internal Review Board of Health Services Academy (HSA), Islamabad, Pakistan, while a supporting letter was also sought from the concerned health administration/department for further research work. The quantitative data were coded and entered into the database of the Statistical Package of Social Sciences (SPSS-21) for analysis and descriptive statistics methods were applied.

RESULTS

Out of 783 inmates (100%), 600 (76.6%) consented to participate in the study; among them three were found HIV Positive. Among them, 368 (61%) prisoners were aged 17-36 years, 398 (66.3%) of them were illiterate and 539 (89.8%) of them were on private jobs. Prisoners who had been in the jail for less than a year were 399 (66.6%), and the prisoners who had been in jail for the longest period, i.e., more than ten years were 29 (4.8%). Moreover, 220 (36.7%) prisoners had been using drugs in their daily lives. Out of these total 220 (100%) drug-addicted prisoners, 19(8.6%) had been using injectable forms of drugs; however, 190 (86.4%) prisoners did not reply. Meanwhile, among prisoners who had been using injectable forms of drugs 18 (43%) conceded that they had been sharing syringes with other drug addicts. In reply to a question regarding the use of condoms during sex, 506 (84.3%) answered they had never used condom during sex. The prisoners who reported surgical and dental procedure history were 29 (4.8%) and 150 (25%) respectively. Moreover, 111 (18.5%) prisoners had received a blood transfusion

in their lives. Furthermore, 141 (23.2%) prisoners stated that they shared razors. Six prisoners were diagnosed as HIV-positive, (three of them were previously diagnosed) hence the overall prevalence (old and new cases) of this study was 1.00%.

The 398 (66.3%) prisons were illiterate/ uneducated, 82 (13.7%) middle school pass, 81 (13.5%) were high school pass while as others having higher qualification were 39 (6.5%). There were 415 (69.2%) married, 176 (29.3%) single and 9 (1.5%) were divorced. We also observed that 225 (37.5%) were Sindhi speaker, 109 (18.2%) were Urdu, 54 (9%) were Punjabi, and other languages speakers were 212 (35.3%) i.e. Baluchi, Seraiki, Pashtoon, and Hindko. The majority of the prisoners 539 (89.8%) were doing private jobs, among them almost were on daily wages, 41 (6.8%) are government servants and 20 (3.3%) are farmers in their occupation and profession in nature.

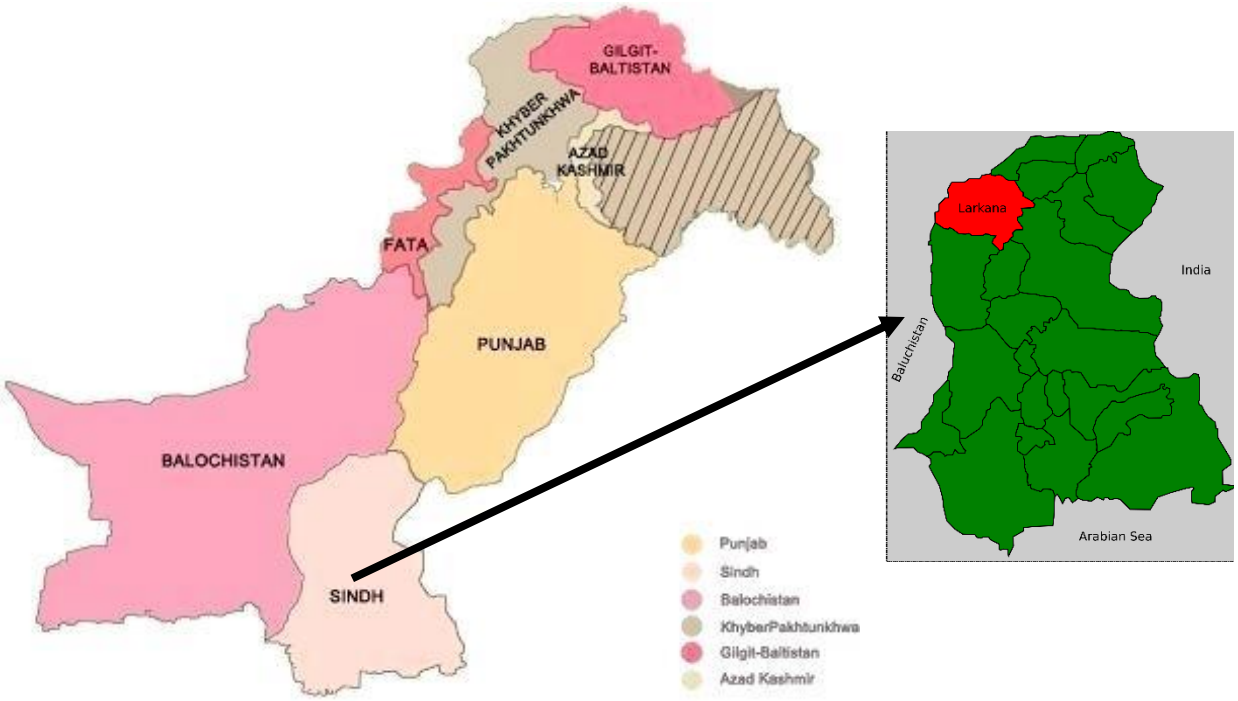

Figure 1. Map of Pakistan (pointer showing the Sindh Province and study district is highlighted in red colour).

Table 1: HIV-associated risk factors among prisoners (N=600)

Drug users	**N (%)**	**Usage of condoms**	
Yes	220 (36.7%)	Never	506(84.3%)
No	380 (63.3%)	Rarely	3(5%)
Type of drug used		No reply	91(15.2%)
Tobacco	138 (72.7%)	**Surgical history**	
Alcohol	19 (8.6%)	Yes	29(4.8%)
Heroin	42 (19%)	No	571(95.2%)
Chavas (Chars)	21 (9.5%)	**History of dental procedure**	
Injectable drugs used		Yes	150(25%)
Yes	19 (8.6%)	No	450(75%)
No	11(5%)	**History of blood transfusion**	
Do not reply	190 (86.4%)	Yes	111(18.5%)
Sharing of syringes		No	489(81.5%)
Yes	18 (43%)	**History of tattoos**	
No	13 (31%)	Yes	53(9%)
Do not remember	11(26%)	No	547(91%)
Age at first time sex		**Same razor usage**	
9-15 years	248(41.3%)	Yes	141(23.2%)
16-22 years	109(18.2%)	No	459(76.8%)

No reply	243(40.5%)	**Usage of condoms**	506(84.3%)
Sex for money		Never	3(5%)
Yes	2(3%)	Rarely	91(15.2%)
No	578(96.3%)	No reply	
Do not remember	20(3.3%)	**Surgical history**	29(4.8%)
		Yes	571(95.2%)
		No	

Table 2: HIV associated risk factors among HIV positive prisoners(N=06)

Drug users	n (%)	**History of dental procedure**	
Yes	6(100%)	Yes	1(16.7%)
No	0(0%)	No	5(83.3%)
Type of drug used		**History of blood transfusion**	
Heroin	5(83.3%)	Yes	1(16.7%)
Chars	1(16.7%)	No	5(83.3%)
Injectable drugs used		**History of tattoos**	
Yes	6(100%)	Yes	1(16.7%)
No	0(0%)	No	5(83.3%)
Sharing of syringes		**Same razor usage**	
Yes	5(83.3%)	Yes	2(33.3%)
No	1(16.7%)	No	4(66.7%)
Age at first time sex		**Sex for money**	
9-15 years	2(33%)	Yes	0(0%)
16-22 years	4(66%)	No	6(100%)
No reply	0(0%)		
Usage of condoms		**History of surgery**	
Yes	0(0%)	Yes	1(16.7%)
No	6(100%)	No	5(83.3%)

DISCUSSION

The study revealed that the most of prisoners were young,i.e. 17-36 years, whereas in another local study, most of the prisoners were in the age range between 15-45 years (17). Another similar study revealed that prisoners more than 50 years of age were the lowest in number among all age groups (18). The results show that the illiteracy rate was very high among prisoners, in contrast to the findings of another study which revealed that 36.5% of inmates were illiterate (18). As illiteracy often leads to poverty, our study revealed that the economic condition of prisoners was also debilitated as a majority of them had earned livelihood through daily wages. The ratio of drug users among prisoners was also high as more than one-third of them stated that they had been using drugs; whereas a similar study conducted in Brazil reported still a higher percentage, i.e. 61% of inmates had been using various forms of drugs (19). However, the majority of them did not reply to the question regarding mode of drug usage. Therefore, chances of high prevalence of injectable drug usage among the prisoners cannot be ignored. Out of 42 (100%) prisoners, who said that they had used injectable drugs, 18 (43%) stated that they shared syringes with other drug addicts. This statement of theirs implies that they had been at high risk of developing lethal diseases such as AIDS. Meanwhile, with regard to syringe sharing, a previous study reported that half of the study participants had a history of sharing syringes for drug addiction (17). Moreover, the study reveals that early-age sex was not uncommon in the study participants as 248 (41.3%) of the respondents had their first sex in age between 9-15 years; this finding is almost similar to that of a previous study conducted in Karachi where 45.9% prisoners had reported early age sex (20). Also, a large number of prisoners were at risk of sexually transmitted diseases (STDs) including HIV/AIDS due to non-usage of condoms as 506 (84.3%) of the study participants had never used condoms during sex. The overall prevalence of this study was 1.00%, similar to two previous studies that revealed the prevalence of HIV among prisoners as 1% and 1.58% (19, 20). The results revealed that majority of the study participants did not have significant past surgical or dental procedure history. Meanwhile, 111 (18.5%) of the total screened prisoners replied that they had received blood transfusions in their lives; lower percentage of similar finding was noted in a previous study (17). Same razor usage was also not uncommon practice in the lives of prisoners as 141 (23.2%) told they had been using razors used also by other persons, whereas 26% inmates shared razors according to an earlier study (17). We observed that the prison was overcrowded,

which is similar in other prisons in Pakistan, and worst in caparison with rest of the world (21, 22). The overcrowding, and poor living conditions can have negative impact, HIV-positive prisoners are not kept separately to prevent others from spread of HIV, which is not different from the jails for females (23, 24).

STRENGTHS AND LIMITATIONS

Our study has several strengths as well as some limitations. We used cross-sectional study design which is useful for description. The primary investigator along with research assistants collected the data on a pre-designed standardized questionnaire form and interviewed the subjects. Our study was conducted in one prison facility of the Sindh province and the country, whereas the situation in other facilities may be different in other prison facilities. For injectable drug used and age at first sex majority (86.4% and 40%, respectively) of the participants did not reply, hence the non-response rate was high, which may have made the results somewhat biased. Other limitations include the absence of a comparative group and limited time for the study. Since our results may not be generalized to the entire ninety-eight prison's population in the country, further studies with larger population and/or multicentre facilities are necessary in the other geographic areas.

CONCLUSION

High prevalence of HIV risk factors, i.e. drug addiction, intravenous drug usage, sharing of syringes and razors as well as unsafe sexual practices were found among the prisoners. Most of the prisoners were also less educated and economically unsecure. There is dire need to conduct health awareness sessions, with particular focus on sex education, in the prisons. At the same time, vocational training programs should be introduced in the prisons so that, prisoners released from jail can live a better and hygienic life. Additionally, there is need of assessing prevalence of HIV and associated risk factors among prisoners in a broader study setting.

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Authors' Contributions:

MHS has participated in study design, data analysis and interpretation, draft writing, editing and submission. KA and MM participated in study design, data collection, data entry, data interpretation and editing. SAS, MI, TFM, SHK, SP and SM participated in study design, data interpretation and editing. All authors read and approved the final manuscript.

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ORIGINAL RESEARCH

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Phytochemical analysis and Antidiabestic activity of *Withania somnifera* and *Cnidium monnieri* using Animal Models

Muhammad Jahangeer[1,3*], Naveed Munir[2,3], Areej Riasat[3], Azka Maryam[4], Shoukat Hussain[3], Alia Ambreen[3], Sumia Urainab[3], Zahed Mahmood[3], Umair Khalid[3], Muhamma Shaheen Iqbal[1], Mehvish Ashiq[5]

1. Food and Biotechnology Research Center, PCSIR Laboratories Complex Ferozpur Road Lahore
2. Department of Biomedical Lab Sciences, School of Health Sciences, University of Management and Technology Lahore
3. Department of Biochemistry Government College University Faisalabad, Pakistan
4. Department of Chemistry, University of Lahore, Punjab, Pakistan
5. Department of Chemistry, The Women University Multan

Corresponding Author
Muhammad Jahangeer
Email: rajahangeer@gcuf.edu.pk

ABSTRACT

Type 2 diabetic is a chronic, non-contagious disease with serious complications. The progression of excess weight leads to the increasing incidence among populations of diabetes mellitus type 2. In form 2 diabetes mellitus instances the median input of obesity is 90%. Moreover, around 174 million individuals worldwide are subject to glucose intolerance, the most prevalent being obesity and metabolic syndrome. There are many therapeutic plants in the medical field and out of these *Withania somnifera* and *Cnidium monnieri* are effective against many disorders such as allergy reactions, dermatophytes, many types of bacterial and fungal infections, osteoporotic, weakness, coldness, and skin-related disorders. This study aimed to check out the hypoglycemic, obesity prevention, cytotoxic & hepatoprotective activities of these two plants. The animals were divided into 7 groups, the first group was a normal controlled group and second group was intoxicated. The third group was treated with standard drugs Glucophage and Mevastatin. Rats of fourth, fifth, sixth, and seventh group was treated with extracts of *Withania somnifera* and *Cnidium monnieri* in high and low concentrations. As expecting these both gave positive results showing the significant decrease in body weight led to a decrease in insulin level and also had cytotoxic effect that was close to normal value.

Keywords: *Withania somnifera*, *Cnidium monnieri*, Diabetes, Obesity, Phytochemical analysis, Cytotoxicity

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INTRODUCTION

Diabetes is characterized by improper metabolic symptoms of numerous conditions, known as long-term poor glycemic control, & results in impaired glucose, lipid, also protein metabolism due to reduced insulin production or insulin performance. At that time, important interventions in the development of science and technology as well as advanced medical centers were observed, protecting humans from the risks of many skin lesions and prolonging the life of the world. These interventions lead to cumulative death in the world, completely changing the epidemic and turning the epidemic aspect into an incurable disease. Over 70% of deaths throughout the world are expected to be caused by widespread diseases. There are many complications associated with type 2 diabetes, which is one of the most prevalent non-contagious diseases (1).

A large portion of diabetes cases is caused by aging populations and obesity rising at an alarming rate. The global shift in lifestyle exacerbates harmful health practices, such as inactivity and poor nutrition. There is a growing epidemic of diabetes around the world, both in wealthy and poor nations. There are 8.8% of adults worldwide have diabetes at the moment. The prevalence of diabetes varies by region's demographics, including age, gender, and economic standing (2).

Human illnesses have been treated with plants for more than 60,000 years and crops are used in local programs to treat a variety of diseases. A total of 65% of the

worldwide population has been incorporated into the wellness system by the World Health Organization (WHO) (2003 rules) (see WHO Guidelines). The main role of plants as drugs is 1) bioactive elements are separated and purified and applied as medicines 2) Biologically active compounds are semi-synthesized using this compound to create known structures or new structures and generate less toxicity with high-activity compounds.

The major disadvantage of traditional drug treatment is immunosuppression. In modern medicine, plants are still at an early stage as a basis of immunomodulators. W. somnifera and *Cnidium monnieri* have shown immunomodulatory effects. A chemical compound osthol which is a derivative of coumarine, isolated from C. *monnieri* herbal exist in China. It has been used as a botanical coumarin compound as a glaze and energizer in China. It is effective against many disorders such as, allergy reactions, dermatophytes, many types of bacterial and fungal infections, osteoporotic, weakness, coldness, and skin-related disorders as a result of subcutaneous injection of C. *monnieri* (L.) CUSS alcoholic extract, the mating period was confirmed one day for 21 days of castrated mice. The consequences of this test show that this alcoholic extract containing osthol may possess activities of estrogen (3).

In medical field, *Withania somnifera* is acting as psycho pharmaceutical plant commonly utilized in Bharath and other countries. *Withania somnifera* is thought to be adaptogenic by many herbal doctors and scientists. It is helpful for curing long lasting complication which are due to nervous system or anxiety (4). Recent observations in our experimental dose surveys showed that W. A relatively low daily dose of Somnifera oral extract increases stress resistance in laboratory rats. It shows that the effects of anti-anxiety or antidepressants is increasing in tense rodents with the number of treatment days (5). In this statement, the outcomes of an experiment resulting that test performed in harassed rats might be important to understand the pharmacology of low doses of W. somnifera. however, based on the current understanding of medicinal phytochemicals and phytopharmacology, we have briefly described the original hub and adaptation of biologically active ingredients of adaptogenic plants.

The purpose of this study was to check the qualitative & quantitative observations of *Withania somnifera* and *Cnidium monnieri* (CM). Animal models were used to explore the antidiabestic activity of selected plants compared with some standard allopathic drug.

MATERIALS AND METHODS

Animals handling and dosing

A group of animals of the same age and weight (120-160 g) were bought from the Department of Physiology, Government College University, Faisalabad, and were bred for 21 days. Animals were divided into seven groups and were dosed in a way that the first group was normally controlled group and other groups were induced to diabetes by giving 100-200mg of and were given a high-fat diet. Afterward, the third group was treated with mevastatin and Glucophage (metformin HCL). The remaining groups were given high and low doses of *Withania somnifera* and *Cnidium monnieri* and compared their results.

General methods for blood collection

To check the effect of plant extracts compared with allopathic drugs, animal trials using rats as an experimental model were performed. Rats were dosed with plant extract and protein diet at regular intervals and after three weeks blood sampling via heart puncture and blood test specimens were performed to test for biochemical analysis.

We collected blood specimens by the following methods:

- Anesthesia-free blood collection
- Saphenous vein (rat, mice, guinea pig)
- Dorsal pedal vein (rat, mice)

Phytochemical Analysis

For phytochemical analysis tests for Tannins, Flavonoids, Glycosides, and triterpenoids were performed to evaluate the quantitative and qualitative assay of selected medicinal plant extracts (6). Ferric chloride test, lead acetate test, and saponin's test was used to check out the presence of tannins based on color indication as ferric chloride gave the violet color indication with tannins, and later two gave yellow-brown and white precipitate showing the presence of tannins. Shinoda's test and Alkaline reagent test were used to find out the presence of flavonoids based on color formation as Shinoda's test gave the reddish-purple indication and the alkaline reagent test gave the colorless result with flavonoids. Libermann-Bruchard Reaction, Legal's test, and Borntrager's test was used to check out the presence of glycosides based on color formation as the first one gave blue or red indicator, Legal's test gave the purple or red while the last one gave the purple indication showing the presence of glycosides (7). Libermann Burchard test, Noller test, and Salwoski test were used to check out the presence of triterpenoids based on color formation as the first one gave the reddish violet color, red color was. developed with Nobler's test and the last one gave blue green indication showing the presence of triterpenoids (8).

Biochemical Analysis

The complete blood count (CBC) was conducted to evaluate the blood-circulating (9) cells including White blood cell count (WBC or leukocyte count), WBC differential count Red blood cell count (RBC or erythrocyte count), Haematocrit (Hct), Haemoglobin (Hbg) Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH) Mean corpuscular haemoglobin concentration(MCHC), Red cell distribution width (RDW), Platelet count Mean Platelet Volume (MPV). In order to measure the amount of glucose or sugar in a person's blood, random glucose tests are used (10). Tests that were used to check out either the liver was performing proper functions or not included Alanine Transaminase (ALT) test Aspartate Transaminase (AST) test, Alkaline phosphatase, (ALP) Test and Bilirubin test. A lipid profile test was performed to check out the total cholesterol, LDL, HDL, and triglycerides level in blood (11).

Final sampling

After six weeks, the final sampling was performed. Sampling was performed by providing animals anesthesia. For this purpose, chloroform was used. The animals were then sacrificed for further assessment. Liver and pancreas were detached for biopsy

Phytochemical analysis of *Withania somnifera* and *Cnidium monnieri* discussed in table 1 (qualitative analysis) and in table 2 (quantitative analysis). Phytochemicals such as alkaloids, flavonoids, tannins, saponins, glycosides, steroids, and triterpenoids were present in *Withania somnifera*. Phytochemicals such as falvonoids, glycosides, steroids, triterpenoids were present in *Cnidium monnieri*.

Quantitative analysis of *Withania somnifera* and *Cnidium monnieri* discussed in following table. Analysis results showed in basic units of TPC, TFC, DPPH activity. *Withania somnifera* or Ashwagandha is widely used as a folk medicine to treat multiple illnesses. It is a natural origin of withanolides (steroidal lactones), a phytochemical that is used as a component in many formulations prescribed for a multitude of illnesses. It functions as a sedative, diuretic, and anti-inflammatory agent usually used to increase energy and strength and acts as an adaptogen that functions as a powerful immune stimulator and anti-stress agent.

Medicinal plants retain the health & vitality of people and also heal illness without causing poisoning. The accessible scientific data favor the hypothesis that Ashwagandha is a powerful regenerative tonic due to its various pharmacological activities such as anti-stress, neuroprotective, anti-tumor arthritis, analgesic, anti-inflammatory, etc.

RESULT AND DISCUSSION

Table.01 Qualitative analysis of *Withania somnifera* and *Cnidium monnieri*

Plants/ Phytochemicals	*Withania somnifera*	*Cnidium monnieri*
Alkaloids	+	-
Flavonoids	+	+
Tannins	+	-
Saponins	+	-
Glycosides	+	+
Steroids	+	+
Triterpenoids	+	+

Table 02 Quantitative analysis of *Withania somnifera* and *Cnidium monnieri*

Plants/ Phytochemicals	*Withania somnifera*	*Cnidium monnieri*
TPC (mg GAE/g dry plants material)	179.51 ± 5.63	291.99 ± 8.43
TFC (µg CE/g dry plants material)	35.76 ± 0.53	77.1 ± 0.90
DPPH Scavenging activity (%)	47.41 ± 3.13	36 ± 4.16

Table 03: A Lipid profile Assay of Animal models for different groups. All the results show P value as follows P<0.05.

Groups	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)
Normal	41.03±0.039	10.24±12.49	51.72±8.4	57.21±8.8
Negative control (Intoxicated)	101.5±9.7	18.33±8.4	70.00±11.6	81.79±6.3
Standard Drug	40.02±0.02	11.21±10.47	50.71±9.3	58.31±9.8
WS (Low)	43.8±6.84	8.17±6.64	17.27±5.33	40.6±5.9
WS (High)	51.6±7.51	8.63±11.92	75.17±12.31	52.06±8.2
CM (Low)	44.5±6.89	9.24±11.93	28.33±10.11	44.63±7.6
CM (High)	41.5±6.03	7.91±9.32	26.95±8.2	40.00±5.6

It is helpful for various kinds of illnesses such as Parkinson's disease, dementia, memory loss, stress-induced illnesses, malignancies, and others. *Withania somnifera* root medicine has a significant position in the therapy of rheumatic pain, swelling of the joints, nervous illnesses, and epilepsy. Dry roots are used as a tonic for hiccups, colds, coughs, sexual illnesses, sedatives, senile debility, etc. Leaves are used for carbuncles, inflammation and swelling. Leaf juice is helpful for conjunctivitis. It has anti-inflammatory, anti-tumor, anti-stress, anti-oxidant, mind-boosting, immune-enhancing, and rejuvenating characteristics (12). The current research shows the existence of phenolic compounds, flavonoids and antioxidants in WSREt and WSLEt and also offers evidence to promote the restoration of alloxan-induced diabetic harm in rats (13).

Lipid Profiles

Normal range of Cholesterol, HDL, LDL, Triglycerides were as 41.03±0.039, 10.24±12.49, 51.72±8.4 and 57.21±8.8 respectively, these values were closed to their standard values. When these rats were intoxicated their values were increased in the range of 101.5±9.7, 18.33±8.4, 70.00±11.6 and 81.79±6.3 respectively as compared with the results (14) our study is comparative.

But as a treatment when plants *Withania somnifera* and *Cnidium monnieri* were given the results were obtained as follows. Experiments performed with reference to (15), when *Withania somnifera* was used in low concentrartion Intoxicated rats showed relatively decreased in their Lipid profiles value such as cholesterol value 101.5±9.7 decreased to 43.8±68.4, HDL value 18.33±8.4 decreased to 8.17±6.64, LDL value decreased 70.00±11.6 to 17.27±26.33 and Triglycerides value 81.79±6.3 decreased to 40.6±59.91. When High concentration of *Withania somnifera* extracts was given to diseased rats remarkable changes in their values was observed such as cholesterol level 41.03±0.039 had minutely increased to 51.6±7.51, HDL value 18.33±8.4 decreased to 8.63±11.92 which was closed to normal value, LDL value 70.00±11.6 increased to 75.17±12.31 when a high dose of *Withania somnifera* was given to rats. Diseased rats had shown great decrease in Triglycerides value when extracts of high dose of *Withania somnifera* were given to them, their value decreased from 81.79±6.3 to 52.06±8.2 but this change was not as remarkable as when high concentration of *Withania somnifera* extracts were used in controlling Triglycerides value. When second plant *Cnidium monnieri* (CM) was given to treat the diseased rats, significant decrease in intoxicated rats' values were observed as discussed in the above table. When low dose of CM plants was used cholesterol, value decreased from 101.5±9.7 44.5±6.89, HDL value came in range of 9.24±11.93 from 18.33±8.4, LDL value 70.00±11.6 decreased to 28.33±10.11 and Triglycerides value 81.79±6.3 decreased to 44.63±7.6. But when high dose of CM plant extracts was injected to intoxicated rats, greater differences were observed. Cholesterol, HDL, LDL, Triglycerides values 101.5±9.7, 18.33±8.4, 70.00±11.6 and 81.79±6.3 were decreased to 41.5±6.03, 7.91±9.32, 26.95±8.2, 40.00±5.6 respectively. High dose of CM plants had positive effects in controlling Cholesterol and HDL values in intoxicated rats as compared with the results (16). All the results show P value as follows P<0.05.

Hormonal Test

Normal range of Insulin, T3, T4, THS were 1.63±1.93, 1.63±1.93, 10.37±1.48 and 0.03±0.055 respectively, these values were closed to the values when standard drug was used as in the range of 1.53±1.87, 0.54±0.05, 10.36±1.39 and 0.03±0.049. When rats were intoxicated their normal range, values of Insulin T3, T4, TSH were increased in range of 2.18±.1.62, 1.67±0.115, 16.57±0.51 and 0.66±0.140 respectively.

After intoxication, these rats were treated with our two medicinal plants *Withania somnifera* and *Cnidium monnieri* (CM) in high and low dose trials planned with re comparative study of (17).

Table 04: Hormonal Assays of Animal models for different groups. All the results show P value as follows P<0.05.

Groups	Insulin (mg/dL)	T3 (µg/dL)	T4 (ng/dL)	THS (m U/L)
Normal	1.63±1.93	1.63±1.93	10.37±1.48	0.03±0.055
Negative control (Intoxicated)	2.18±.1.62	1.67±0.115	16.57±0.51	0.66±0.140
Standard Drug	1.53±1.87	0.54±0.05	10.36±1.39	0.03±0.049
WS (Low)	2.34± 0.61	0.38±0.068	7.33±0.711	0.43±0.318
WS (High)	1.59±1.46	0.50±0.03	11.10±1.05	0.05±0.004
CM (Low)	1.50±1.42	0.38±0.05	9.27±0.153	0.34±0.25
CM (High)	1.40±1.47	0.31±0.03	8.03±0.153	0.23±0.015

When the low dose of *Withania somnifera* were given to rats, insulin concentration was not controlled in the normal range, but T3 value decreased from 1.67±0.115 to 0.38±0.068 that was less than normal range of T3 value, T4 value 16.57±0.51 decreased to 7.33±0.711 which was also lower than normal value and THS value 0.66±0.140 decreased to 0.43±0.318. When high dose of *Withania somnifera* were given insulin value 2.18±.1.62 decreased to 1.59±1.46 which was very close to normal value of insulin, T3 value 1.67±0.115 decreased to 0.50±0.03 which was less than the normal range, T4 value 16.57±0.51 decreased to 11.10±1.05, THS value 0.66±0.140 decreased to 0.05±0.004 which was close to normal range value of THS.

When the low dose of *Cnidium monnieri* (CM) plant extracts was given to intoxicated rats, remarkable changes were observed in rats Hormonal profiles as discussed in the above table. Insulin value 2.18±.1.62 decreased to 1.50±1.42, T3 value 1.67±0.115 decreased to 0.38±0.05, T4 value 16.57±0.51 decreased to 9.27±0.153 and THS value 0.66±0.140 decreased to 0.34±0.25, when a high dose of CM plant extract was given to intoxicated rats, and results were close to their normal ranges. After that High dose of CM plant extracts were given to rats and changes were observed as follows.

Insulin value 2.18±.1.62 decreased to 1.40±1.47, T3 value 1.67±0.115 decreased to 0.31±0.03, T4 value 16.57±0.51 decreased to 8.03±0.153 and THS value 0.66±0.140 decreased to 0.23±0.015. High dose of both plants had positive effects in controlling the hormones in their normal ranges (18). All the results show P value as follows P<0.05.

Cytotoxic activities and hepatoprotective

Normal range of Urea, Creatinine, Blood sugar rate and Uric acid were observed as 28.66±40.49, 1.03±1.70, 0.59±0.06 and 2.03±1.58 respectively, these values were close to the values when the standard drug was used as in the range of 27.56± 39.40, 1.02±1.69, 0.58±0.06 and 2.02±1.59. When rats were intoxicated their normal range, values of Urea, Creatinine, Blood sugar rate, and Uric acid were increased in the range of 53.39±72.12, 1.14±1.61, 1.67±0.11 and 5.04±3.87 respectively. After intoxication, these rats were treated with our two medicinal plants *Withania somnifera* and *Cnidium monnieri* (CM) in high and low dose trials (19).

When low dose of *Withania somnifera* were given to rats, Urea concentration 53.39±72.12 decreased to 21.73±33.73 and this value was less than normal value, creatinine value 1.14±1.61 decreased to 1.03±1.71 that was same as the normal range of creatinine value, Blood sugar rate value 1.67±0.11 decreased to 0.38±0.06 which was quite close to normal value and Uric acid concentration 5.04±3.87 decreased to 2.99±1.49 that was also equal to normal range value. When high dose of *Withania somnifera* was given Urea value 53.39±72.12 decreased to 30.12±44.38 which was high than normal value of urea, creatinine value 1.14±1.61 decreased to 1.04±1.70 which was close to normal range, Blood sugar rate value 1.67±0.11 decreased to 0.50±0.03, Uric acid value 5.04±3.87 decreased to 3.68±1.57 which was high than normal range value of Uric acid.

When low dose of *Cnidium monnieri* (CM) plant extracts were given to intoxicated rats, remarkable changes were observed in rats' Cytotoxic activities and hepatoprotective activity profile as discussed in the above table. Urea concentration 53.39±72.12 decreased to 25.85±37.38, and creatinine value 1.14±1.61 decreased to 1.05±1.68. Blood sugar rate value 1.67±0.11 decreased to 0.38±0.04 and Uric acid value decreased to 2.01±1.68 which was close to the normal range value of uric acid.

After that High dose of CM plant extracts was given to rats and changes were observed as follows Urea concentration value 53.39±72.12 decreased to 23.61±32.71, creatinine value 1.14±1.61 decreased to

Table 05: Renal failure analysis of blood samples of animal models. All the results show P value as follows P<0.05

Groups	Urea (mg/dL)	Creatinine (mg/dL)	Blood sugar rate (mmol/L)	Uric acid (mg/dL)
Normal	28.66±40.49	1.03±1.70	0.59±0.06	2.03±1.58
Negative control (Intoxicated)	53.39±72.12	1.14±1.61	1.67±0.11	5.04±3.87
Standard Drug	27.56± 39.40	1.02±1.69	0.58±0.06	2.02±1.59
WS (Low)	21.73±33.73	1.03±1.71	0.38±0.06	2.99±1.49
WS (High)	30.12±44.38	1.04±1.70	0.50±0.03	3.68±1.57
CM (Low)	25.85±37.38	1.05±1.68	0.38±0.04	2.01±1.68
CM (High)	23.61±32.71	1.04±1.69	0.31±0.03	2.40±1.31

1.04±1.69, Blood sugar rate value 1.67±0.11 decreased to 0.31±0.03 and Uric acid value 5.04±3.87 decreased to 2.40±1.31. High and Low doses of both plants had quite positive effects in controlling the Urea, Creatinine, Blood sugar rate, and Uric acid in their normal ranges. All the results show the P value as follows P<0.05.

CONCLUSION

Aging populations in the world and a tremendous increase in obesity played an important role in the development of diabetes. The incidence of diabetes depends on the age, gender, and socioeconomic position of each geographic zone. The prevalence of diabetes is 22% in developing countries and 75 to 79 years in developing countries,19% in the 60- to 70-year-old group in developing countries and underdeveloped countries, and 8% in the 55-64-year-old group in underdeveloped countries (14). The macroscopic vascular complexity of diabetes plays an important role in the increase of arteriosclerosis, as well as in the acceleration of morbidity and mortality and the aggravation of the incidence. Researchers could not find methods of interaction of both diabetes and atherosclerosis. Oxidation due to highly reactive oxygen species is considered the main cause of insulin resistance, vascular complexity and type 2 diabetes mellitus. Requirements include animal, anesthetic agent, surgical blade, small glass rods, surgical scissor, 21 to 25 G needle with 1 to 5 ml syringe and blood sample collection tube (15). the animals were dosed with plant extract and protein diet Then after three weeks re-sampling was performed. Blood samples were gathered by heart puncture and blood test specimens were used. Animals were dosed with plant extract and protein diet After three weeks; re-sampling was conducted. Blood samples were collected by cardiac puncture and blood samples were used. The complete blood count (CBC) is a blood-circulating cell exam. CBC is typically performed using an automated tool that measures multiple parameters, including the number of cells in the blood sample of a person. Phytochemicals such as flavonoids, glycosides, steroids, and triterpenoids were present in *Cnidium monnieri*. The current research shows the existence of phenolic compounds, flavonoids and antioxidants (20) in WSREt and WSLEt and also offers evidence to promote the restoration of alloxan-induced diabetic harm in rats. Impaired glucose tolerance and insulin resistance, as well as being an efficient means of regulating glucose levels.

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REVIEW ARTICLE

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Prospective of Nanotechnology Application for the Treatment of HCV

Muhammad Jahangeer[1,5], Zawar Hussain[2], Azka Maryam[3], Areej Riasat[4], Alia Ambreen[5], Shoukat Hussain[5*], Zahed Mahmood[5], Wasfa Batool[5], Mahvish Ashiq[6], Sumia Urainab[5]

1. Food and Biotechnology Research Centre, PCSIR Laboratories Complex Ferozpur Road Lahore
2. Centre of Excellence in Solid State Physics, The University of Punjab Lahore
3. Department of Chemistry, University of Lahore, Punjab, Pakistan
4. School of Biological Science, The University of Punjab Lahore
5. Department of Biochemistry, Government College University Faisalabad
6. Department of Chemistry, The Women University Multan

***Corresponding Author**
Shoukat Hussain,
shoukatdaha765@gmail.com ‘

ABSTRACT

Chronic Hepatitis C infection is a common worldwide disorder, caused by Hepatitis C Virus (HCV). Right around 180 million individuals are affected by Hepatitis C Virus infection globally and more than 50 million in South Asia. Ribavirin and interferon are used for many years for the treatment of HCV, direct acting agents, and combination therapy as well. The main problem with these therapies is that a lot of side effects are observed. A novel procedure is utilized for the treatment of HCV which is called nanotechnology. The major advantages of those technology are that there is no wastage of drugs and avoid the hydrolysis of drugs. Different kinds of the bearer are utilized as a part of the treatment of HCV like nanoparticles, bio-conjugation, micelle development and dendrites. Diverse sorts of Nano transporters are utilized that convey the medication stacked particles to target points and diminish symptoms. According to this description, the part of nanocomposite like a transporter for anti-hepatitis C virus vaccine, anti-hepatitis C virus deoxyribozymes, anti-HCV aptamers, anti-HCV phenolic compounds and their focused-on conveyance are talked about. Additionally, nanoparticles give a different strategy to antigen conveyance, which not just actuates distinctive components of the same framework yet, in addition, has great biocompatibility.

Keywords: Nanotechnology, Hepatitis C Virus, Bio-Conjugation, Biocompatibility, Nanoparticles

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INTRODUCTION

Hepatitis C virus (HCV) has been referred to all around as the essential purpose behind unending liver disorder (1). Hepatocellular carcinoma, liver cirrhosis, and end-stage liver disease are all associated with HCV infection, which ultimately results in death (2). Up to 3% of the total people, around 200 million people are assessed to have HCV disease. Among every one of the general populations contaminated with HCV, there are no less than six genotypes because of the higher inaccuracy level of RNA-subordinate ribonucleic acid polymerases among hepatitis C virus replication. Genetic constitution 1 (G1) is mostly prodigious on the universe (almost 83.4 million individuals) straggled by G3 (3) at that point Genotype 2, Genotype 4, Genotype 5 and Genotype 6. HCV spread predominantly happens through damaged blood and blood transfusion, infusion medicate utilize, haemodialysis and transplantation; anyway, undefended sex and delivery subsequently a contaminated mother will have likewise recorded as different methods of spread (2).

HCV is a single *Flaviviridae* infection family, which remains an encompassed certain single-stranded RNA infection. Just about 9600 bases are available in the HCV genome, which shapes a constant uncovered perusing outline circumscribed by 5' and 3' non-deciphered locales. Inward ribosome section

destinations (IRES) are available in the 5' non-interpreted area which is important to begin the interpretation of the HCV genome. Around 3000 amino corrosive polyprotein forerunners are delivered by IRES– intervened interpretation (4). Developing viral auxiliary and non-structural (NS) proteins are in this manner cuts co-and post-translationally by IRES–intervened interpretation.

The cleavage treatment of the polyprotein is finished by cell peptidases (5). And two widely used proteases, NS2/3 & NS3, cause breaks into 10 precisely defined subunits: NS proteins namely NS4A and NS4B, NS5A and NS5B, and basic Core (C) of particle channel p7, NS2, NS3, envelope proteins (E1 and E2), Despite the reality that E1 & E2 get the enveloping glycoproteins, subunits E1, E2, and C form the infection subunits in whose nucleocapsid is generated from repetitive copying of the centre protein. A protein called NS that frames NS5B, the viral replicator complex, is responsible for delivering the non-structural protein (NS3). Furthermore, the RNA polymerase is also shaped by the NS5B protein (6).

These Nanoparticles proceeded in the liver relate for 7 days post-infusion (when consolidate with regular IFN-α and PEG Intron), in this way commitment enhanced likely to improve things and delayed treatment of HCV contamination. Understood outcomes indicating >99% HCV hindrance was characterized. Some place Nano-proteins stayed produced by methods for gold nanoparticles functionalized over RNAse and against HCV glycol-nucleotides, for dynamic breakage of hepatitis c infection arrangement particular RNA in together cell belief systems and mouse representations (7). These nano-compounds likewise offered to remarkable commitment in conundrum of proteinase awful conditions, genuine disguise, and great harmfulness designs. In an alternate direction cross-connected polymeric micelles (CLPM) were utilized to segregated hepatitis c infection in vitro. The micelles were prevented with the recently acknowledged intense hostile to HCV complex, camptothecin (CPT), this is additionally related with parameters, for example, reduced water solvency and compound instability. The CLPMs tradition in this portrayal reasonable the advance of appropriate amphiphilic micelles including a hydrophobic boss and hydrophilic covering, which perceived exceptional stacking limit with regards to CPT while support HCV antiviral exertion and dropping cytotoxicity (8).

Introduction of nanotechnology

Nanotechnology is the formation and consumption of supplies, strategies, and organizations through the regulator of matter on the nanometre-length scales, i.e., at the side-by-side of atoms, molecules, and supramolecular arrangements. Nanotechnology, as precise by the National Nanotechnology Initiative, is the considerate and control of substances at proportions of evenly 1 to 100 nanometres, where distinctive spectacles permit different presentations (9). About nano-scale discipline, production and knowledge, nanotechnology includes imaging, calculating, demonstrating, and employing matter at this extent scale. It is the general term for the building and consumption of useful arrangements with at smallest one representative measurement slow in nanoscale or nanometre is one fraction of a meter (10-9 m). Explain the role of Nanotechnology in dissimilar areas of biological and biomedical sciences are given as;

- Improvement of viral diagnostics (finding of single viral constituent part)
- Observing antiviral rehabilitation
- Addition of therapeutics with diagnostics (modified treatment)
- Study of collaboration of nanoparticles with viral particle
- Nano coating for native viricidal consequence
- Development of antiviral agent's transport
- Fullerenes as antiviral mediators
- Nano-viricide approach for the destruction of the virus

Viral nanoparticles

Examination of viral-related nanoparticles has offered signs to the suggestion of cytoplasmic movement. Infections that imitate their genomes in the middle make the procedure of the microtubule and the actin cytoskeleton as sub-atomic engines for transporting toward the atomic sheath amid entrance and the outskirts through outlet after replication. Investigative the principal philosophies of viral cytosolic movement will be useful in the arrangement of viral vectors to be used in examination and also human quality restoration and in the sensitivity of new antiviral article atom set (7).

Mechanism of action of ribavirin HCV antiviral therapy

A manufactured nucleoside is Ribavirin which is mechanically identified with guanosine. Ribavirin quickly goes into the eukaryotic cells, in the wake of entering it attempts intracellular phosphorylation, displays movement of virus growth stop against a wide range of RNA and DNA infections (10). The correct component of ribavirin which played out the antiviral activity has not anyway been totally explained.

However, a few investigations propose the accompanying conceivable instruments:

- Straight hindrance of HCV duplication.
- Reticence of the chemical inosine monophosphate dehydrogenase of the swarm.
- Initiation of mutation in the viral RNA.
- Immunomodulation through the acceptance of a Th 1

(Th1)- kind resistant reaction RBV is quickly ingested (half-existence of around 2 h) and broadly circulated all through the body after its oral organization; its utilization happens chiefly by means of the kidneys (11).

There are a few components of activity expressed for ribavirin, each with some investigational confirm; all things considered, the central antiviral instrument obligated for ribavirin movement has been mysterious. A few components partaking to this region of logical difference and contain the way that ribavirin indicates antiviral movement against a few infections with those with RNA and DNA genomes (12). It is far-fetched that one system can be obligated for these perceptions. In including, ribavirin's utilization in HCV treatment is dependent on administration with interferon. Since patients are not treated of HCV with ribavirin monotherapy, communications with the multifaceted antiviral movement of interferon-a, the powerful antiviral operator in the regimen, confounds examination of ribavirin's commitment in mix treatment. (13) Explain break down the request to understand each of the proposed components of activity of ribavirin against HCV, the capacity of ribavirin to apply its antiviral impact either by an immediate instrument focusing on the infection or by an aberrant system focusing on have cells is talked underneath.

Action of mechanism of interferon

The patients with incessant hepatitis C are treatment by cutting edge essentially in current years. Yet, it is calm in view of the utilization of interferon (IFN-α) as an immune-modulatory and antiviral operator against the (HCV) hepatitis C infection. The interferon alpha remains normally created by the lockups of the resistant system; IFN-alpha will be a group of proteins. The interferon alpha protein presents anti-proliferative, antiviral and immune-modulatory action. In the component, impacting cell division and development, and in addition altering some safe framework performants of natural undertaking happens over the incitement of unequivocal qualities. Subsequently, IFNs have an auxiliary antiviral impact on hepatitis C infection. Modern, IFN-alpha is shaped by assets of two different source of DNA strategies and is accessible in combination of binary diverse subtypes that can be joint through different particles, for example, polyethylene glycol or, all the more as of late, egg whites.

The fluctuation among IFN-alpha 2b and IFN-alpha 2a is in the amino corrosive existing at protein at the situation of 23: IFN-alpha 2a has a lysine, while IFN-alpha 2b has an arginine at that position. A while later the required by its particular receptor (IFNAR) arranged outside of the objective lockups, IFN-alpha invigorates in the cell motioning course, which advances the commencement of IFN-fortified qualities (ISGs), making a non-infection particular against virus formal secret the cell (3). The essential flagging hardware utilized by IFN-alpha is the supposed Janus kinase transducers and enhancers of translation (Jak/STAT) way. Along these lines, two cytoplasmic proteins by the action of tyrosine kinase enzyme related through IFNAR, initiated Jak1 and tyrosine kinase 2 (Tyk2), stay enacted by the dimer formation of the receptors (32). Enacted Jak1 and Tyk2 accomplish the addition of phosphate in STAT1 and STAT2, correspondingly. This binds to another protein p48 building up interferon-empowered quality factor 3 (ISGF3), which translocates addicted to the core and associations with interferon-animated administrative component in the game plans which help an assorted diversity of qualities inducible by IFN-alpha contain proteins against a virus like as 2'5'-oligoadenylate synthetase (2'5'OAS), protein kinase RNA, and Mix protein. The commitment of IFN-alpha (2a or 2b) is unprecedented once overseen hypodermically. The breakdown and end of IFN happens chiefly through the kidneys, with a half-existence of 3-7 h (14).

Recent advances in nanoparticle design

Petros et al (9) stated that enlighten that the main battled combination of a built best nano-particle can be laid out posterior to the 1950s if more prominent than 50 years of training to fascination on in the typical methodology of the present-day arranged nanoparticles. The past time has acknowledged stimulating the step of novel recognitions, selected of which are accentuated below. Almost imperative late advancements in building tiny particles have emerged in the territory of atom form and this one outcome on cell disguise and development periods. Current distributions demonstrate the outcome that molecule form can require cell disguise Like, the result of shape and parameters of association of circular and non-round polystyrene little particles all through eating by alveolar phagocytic cell was considered. Through egg-molded, plate formed little particles, it was found out that when the macrophage first called particles close to the significant arrangement, the particles were immediately received (< 6 minutes) (15).

- **Matrix chemistry**

The huge advancements have recently been finished is in the plan of jolts responsive movers. Constituents might be incorporated that answer either to an inside inspiration (like diminishing the cytosolic in nature related with the outside the cell planetary or the plummet in pH recognized to emerge in endosomes), or with an outer inspiration (like a connected attractive field and scope to an exact frequency of light). Those inspirations remain reused as starts to sever cross linked bonds in the middle of the transporter and shipment, or to undermine the bearer encouraging issue of its internal parts once the bearer has achieved correct area.The lessening idea of the cytosol is utilized widely in protein– conjugate science to generate arrival of the load on cell disguise with loads running after oligonucleotides to poisons and chemotherapy (16).

- **Cellular targeting**

Apparatuses for focusing on cell populaces have been broadly created. This is valid for both specific and non-particular dynamic focusing on techniques and has been expert utilizing different ligands, including antibodies, aptamers, peptides, and little particles. These strategies solely focus on layer bound protein (one exemption is focusing on sugars on the surface of tumour cells with lectins; purported switch lectins focusing on) (17). Dynamic, non-specific focusing on techniques for oncology applications that are coordinated and no more quickly partitioning cells centre fundamentally around folate and transferrin receptors. Even though these receptors are globally coordinated, growth cells routinely slightly higher compared their presence. Recently, the roles of folate and transferrin in targeted medicine administration have been studied. However, it should be mentioned that ligands targeting the transferrin receptor exert their effects via increasing the uptake of targeted nanoparticles (NPs) by cancer cells rather than by increasing molecule accumulation in the tumour region. Once more, because these receptors are communicated to some degree on numerous sorts of non-target cells, lethal off-target impacts can happen (18).

- **Organelle-specific targeting**

Eventually, the viability of any designed nanoparticle will rely upon the productivity of the transporter to convey its load to the intracellular site of activity. For instance, bearers containing oligonucleotides as load, which need to cross the atomic layer to be viable, can be effectively focused to particular cells and disguised. In any case, if they don't get away from the endosome, the oligonucleotides will likely be corrupted under the cruel lysosomal conditions. This features the requirement for procedures to coordinate built nanoparticles to particular subcellular compartments. Instruments and standards for powerful organelle focusing on are raising, for example, those for focused delivery to the core, cytosol, mitochondria, peroxisomes and endosomes/lysosomes (19).

Mechanism of action of drug loaded nanoparticles

Through receptor-mediated endocytosis, medication-overburden NPs are delivered towards the cytosol and specifically focused on organelles. Nanoparticles are encapsulated in a vesicle that is thought to be an initial endosome following receptor-encouraged cell interaction with NPs. Endosomes are alerted to via cytoplasmic release of nanoparticles having an endosome-irritating characteristic. In contrast, if NPs enter early endosomes, they could go forward as late endosomes into the lysosomes, wherever their deterioration takes place. A little portion of non-debased medicine that is present throughout the cytoplasm works informally with cellular components. By and by, cytosolic delivery of a small amount of organelle-focused on nanoparticles by means of endosomal emanation or from lysosomes goes to the focusing on organelles to convey their restorative freight (20).

The road has been lengthy and convoluted from the potential of clinical sufficiency of liposomes towards their proper position in customary of medication distribution frameworks in current decades. The liposome structures have been discovered in the centre for descriptions as various as areas of imaging and contamination, quality delivery, for immunization, and minor atomic treatments, for management of illnesses and for the cancer treatment, for respiratory and skin infection, among others. While there are now many liposomal therapeutic options accessible, rare and beautiful ones are still being used to cure ailments. Because they are simple to use, standard methods for lowering liposome size are still used (21). However, it's not like all research center scale systems are straightforward to scale up for the production of mechanical liposomes (22).

Numerous customary strategies, for getting ready little and vast unilamellar vesicles, include utilization of either water miscible/immiscible natural solvents or cleanser atoms. The requirement for enhancements in the outline and steadiness of liposomal analytic and remedial frameworks will keep on motivating inventive and effective courses to their creation (23).

Advancement in the treatment of HCV

FDA-approved drug Ribavirin is a convincing nucleoside basic as a piece of the treatment of endless HCV nearby IFN. Many examinations used nanotechnology to endeavor and deal with this issue. For instance, red platelet cells have a limited take-up of NPs and lack an endocytic device **(**24**)**.

Polyglycerol adipate and acylated Polyglycerol adipate nanoparticles are utilized as a transporter for RBC boronic destructive, as opposed to using ribavirin just, for this outfits ribavirin with aqua phobic and extend the nanocomposite ' drug stacking capability. The novel, enduring, biodegradable nano-complex exhibited a twofold limit of concentrating on hepatocytes and oversaw the landing of ribavirin (in PBS has 37 days and 7 days in mice after intravenous implantation). This nano-formulation is required to indicate high anti-viral development and then reduced the undesirable special effects of ribavirin **(**25**)**.

Nanoparticles as a transporter for anti-HCV Small interfering RNA

Ribonucleic acid impedance (RNAi) is a small meddling 21 to 23 nucleotides twofold RNA fragment that would reduce is able to quality articulation through overseeing mRNA corruption in a grouping particular way, and its component relies upon post-transcriptional quality hushing. In Huh-7 cells containing the genome of HCV, RNAi may effectively prevent RNA replication and protein assembly of HCV, and the effect antiviral is independent of interferon siRNA experiences a few issues including low cell take-up, quick debasement by nucleases and also insufficient blood dependability, such huge numbers of studies have utilized nanoparticles to take care of these issues and to limit the unfavourable impact of "off-focusing on" (26).

The small interfering RNA-DG framed a steady intricate that needed aim situated distribution through the cooperation among galactose deposits and the receptor of Asialoglyco protein. NS5b and NS3 in viral proteins are co-restricted in small interfering RNA (26).

Nanoparticles as carrier for anti-HCV deoxy ribozymes

Deoxy ribozymes (DNA enzymes) are deoxyribonucleic acid cutting, DNA particles that can separate RNA in a progression specific way (27). They are tremendously viable under imitated physiological circumstances, more moderate from siRNA, and that can be easily falsely improved and then RNA (28). Press oxide appealing nanoparticles used for DNA enzyme Dz681 decided for HCV NS3 RNA centring despite cell entering peptide (MPAP) as an against HCV Nano formulation. It has novel potential as a device in the of HCV treatment (29).

Nanoparticles as carrier for HCV protease inhibitors

A novel nano formulation combines the HCV protease enzyme with anti-fibrotic, anti-hemolytic, and viral section suppressor agents using a combination of naturally occurring non-anticoagulant glycosaminoglycans (GAGs) and thiols/polyphenol (30). For targeted delivery of antiviral drugs, medication-stacked NPs were united to mAb neutralizer components coordinated next to epitopes stored on the HCV exterior genotypes 1a and 1b, 2a and 2b, and 4 of E2 glycoprotein (31). Thus, the nano-fuse of polymerase inhibitors and PIs in addition to anti-fibrotic/anti-homolytic and viral section antagonists considers excellent antiviral survivability and perfect health profiles.

Nanoparticles unaided as an anti-HCV

A class of polyanionic carbosilane dendrimers which can suppress the contamination of HCV in tissue culture has been identified **(**32**)**. G2-S24P was the finest of these mixtures. By interfering with extracellular translocation during the early stages of the viral section, it prevented HCV infection by over 80 percent. Furthermore, it demonstrated an extra material effect when combined with the drug called sofosbuvir (33).

Nanoparticles as a carrier for HCV vaccine

By reducing these in a cationic liposome, CpG-oligodeoxynucleotide was enhanced in its ability to function as an immunomodulatory or adjuvant coupled with transgenic HCV NS3 as just an HCV vaccination model. They demonstrate that the ideal reaction to HCV NS3 was perfectly ignited, not just in cells but also in overly humeral tissues (32). It strongly elicited a protective in refinement Th1 response to HCV. In the study on animals, mice were either given 50 milligrams of GpC or CpG or 10 milligrams of the transgenic HCV NS3 proteins using competent frames or positively charged liposomes in a variety of shaped epitomized forms (34). Every week lasting approximately two months following vaccination, models were produced. Mice injected with liposome-NS3 or liposome-NS3-CpG were intended to cover more IFN-producing cells 1:4 than cloaked IL-4. In animals inoculated with free-NS3, the cells masking interferon were only one-sixteenth the size of the cells masking IL-4, indicating that liposomes containing NS3 alone via CpG can shift the protective responsiveness to HCV NS3 from such a Th2 to a Th1 approach.

Nanoparticles as carrier for phenolic compounds

The ardent polyphenolic regulator of drain thorn, silibinin, has been given the task of preventing HCV infection duplication and transmission, but it has also been shown to have decreased water bioavailability and solubility. According to (31), a group of enzymes may be used as a nano-vector to solubilize and distribute silibinin.

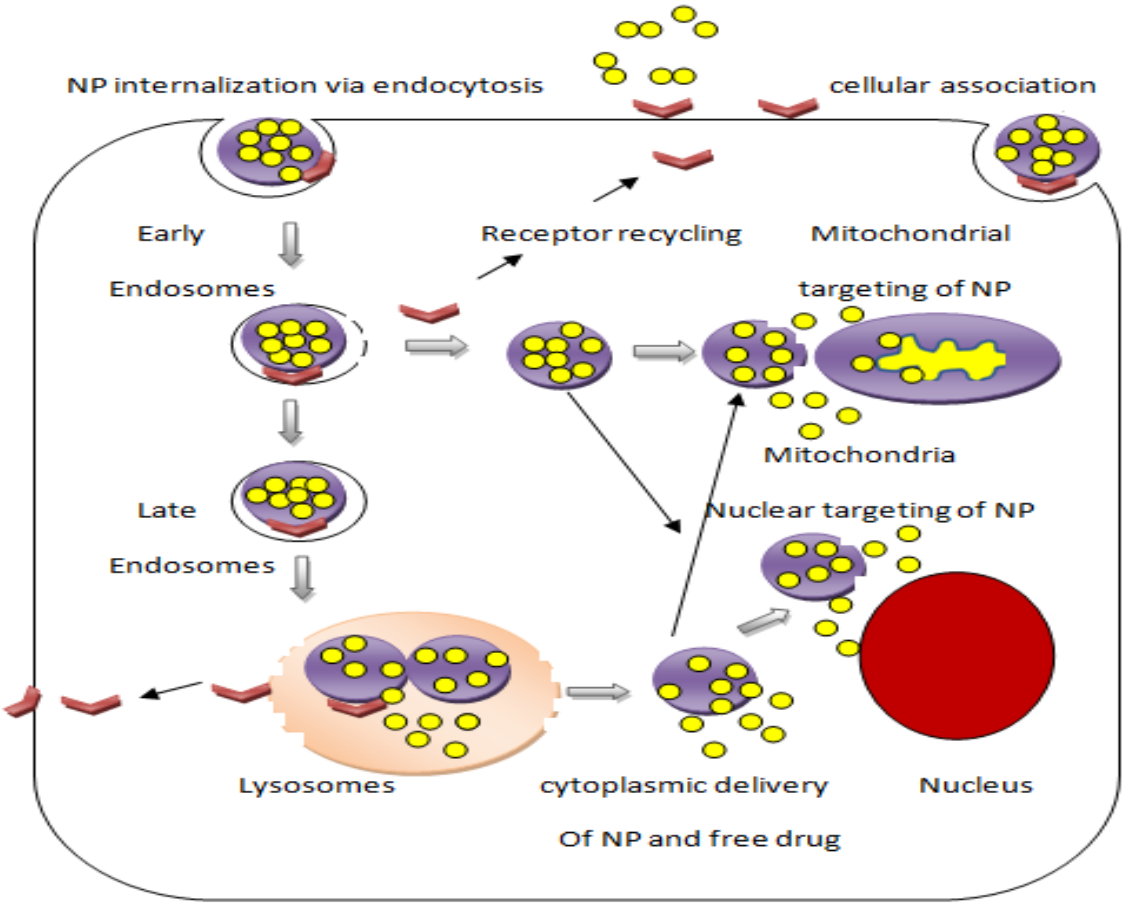

Figure 1. Action of mechanism of drug loaded particle

The suggested NPs were beginning to be non-toxic and had extraordinary anti-virus action to prevent entry with special excitement by hepatocytes.

Lipid nanoparticles as RNAi carrier's infections

As said more than, a great transport system ought to be created for abusing the quality calming by RNA impedance strategy for antiviral treatment (35). In recent years, the importance of lipid NPs for the management of chronic illnesses has increased. The RNAi technique requires specific value groupings and the most fundamental progress for a productive viral deterrent (36).

It is crucial to lay out siRNA against exceptionally apportioned groupings of the viral genome remembering the true objective to streamline feasibility in stifling a bigger piece of contamination strains. The use of neighbouring antibodies to dsRNA agonists as a RIG1 agonist as well as to promote the creation of a DNA vaccine over influenza is known as RNAi adjuvant approach.

Regardless, genotype self-ruling choices should be all the more convincing in the treatment and neutralizing the activity of damage liver. In such way, the RNAi development is an engaging framework (37). This disease's single-stranded RNA has the same properties as mRNA, making it a promising quantity for RNA interference-based therapy. Several studies demonstrate effective HCV replication limitation by employing siRNAs targeted against advancements in the protein-coding regions of emphasis, NS3, E2, NS4 or NS5B.

In any case, these viral coding groupings prolonged assortments among different HCV genotypes. Along these lines, significantly directed regions, for instance, 5′ untranslated zones (5′ UTR), have all the earmarks of being better concentrations for working up a rational antiviral system (38). Given the great selectivity of RNAi and the prolonged therapy, the limitation of all these novel techniques is in the development of suitable disease types. The 5' UTR's inward ribosome portion location is where the proteins of virus bind, facilitating viral replication (39).

Changes to these structures may result in the loss of constraint, providing IRES an amazing quantity for HCV medication antagonists, which may prevent viral egress; it has also been impacted by that of the RNAi

development (40). Another credibility to reduce safe varieties is the blend of no less than two RNAi iotas with different specificities cantered to segregated locale of the HCV genome. Another well-known method for maintaining the change of resistance is to focus on certain regions of both the HCV genome associated host features necessary for contamination propagation (41).

In order to create liver-specific siRNA transporting carriers, (40) used human plasma-derived apolipoprotein A-1. It has been suggested that this protein, a portion of greater thickness lipoprotein, acts as a focusing on ligand for hepatocytes. Following intravenous connection, the lipid-based structures that comprise HCV concentrate on the particular siRNA into such an HCV rat. In a similar study, the engineering modification of the HCV-target particular siRNA to create its serum stable quality attained excellent calming sufficiency approximately to 95 percent for at least six-days (42). The use of rhapo A-1 to transfer siRNA towards the liver was successful and produced specific and compelling apo A-1 obtained from plasma, without affecting the typical hepatic limit (43). In a first work, nano vectors were enhanced the extent that lipid-to-siRNA extent and positive particle measure dependent upon sonication time. Cell appropriateness was kept up around 90% and HCV limitation came to about 85%.

Reiterated treatments and two-siRNA treatments were distinguished from a single siRNA intervention by (40). After using a key combination in a liver tumor rat model of HCV, a fundamental restriction of pathogen replication was obtained. Whenever the combinatorial method was applied, a decline in the modification of acceptable mutants again for management of siRNA was seen. More recently, short generated shRNAs (called sshRNAs) that target a group within IRES have indeed been integrated into LNP by the method of incremental ethanol depletion and unrestricted vesicle development. At 35°C, shRNA was introduced to a liquid mixture comprising 30 percent ethanol after being isolated in a separate solution. After completing the final sshRNA to lipid degree, the mixture was tortured for 30 minutes at 35 degrees Celsius to enable vesicle remodelling and RNA amplification (44). LNP were then channels disinfected through with a 0.2 micrometre channel after being dialyzed using PBS. The intravenous insertion of this vector enabled enough standby the hepatocytes to muffle high-quality verbalization quickly and intensely completely.

The worldwide clinical-sort out biopharmaceutical association Santali's Pharma A/S has developed a threatening to miRNA calm confident starting at now for the treatment of HCV illnesses (Miravirsen, SPC3649) (45). This drug requires for the replication showings against MiR-122, that the HCV. Results first from Phase II a basic showed that Miravirsen, administered as weekly subcutaneous implantable devices more than a month, was generally well tolerated by individuals with persistent HCV genotype 1. (46) Long after the dynamic therapy was finished, antiviral effects persisted and was delayed. These results provide clinical proof of Miravirsen's efficacy as once-weekly treatment for lifelong Hepatitis C virus.

Nanoparticles as carrier for anti-HCV aptamers

Aptamers is a solitary beached oligonucleotide succession, RNA / DNA, and can connect with remarkable partiality to a broad scope of goals, for example, proteins, peptide, medications, and whole cells and infections reliant on their specific restricting sacks for the objective particle (47). Nanomaterial-based aptamers bio conjugates have created significant consideration and a wide assorted variety of employments in medication. With an end goal to consequently lessening the HCV stack in plasma. Arranged a specific attractive nano-conjugate for HCV taking care of utilizing an aptamer (Apt-E1E2-6) for HCV E1 E2 glycoproteins. HCV particles are productively destroyed by aptamer-conjugated attractive nanoparticles and reduced the viral titter from plasma of human illustrations (14).

Advantages of Nano-viricides

Nano-viricides medication contestants are presently in preclinical description. Medical trials are calculated. Firstly, injectable produces are careful to be most operative but other routes of managements like nasal sprays and bronchial aerosols can too be (48). Various nano-viricide outcomes will be defined more along with appropriate viral diseases.

Nano-viricides have been likened to current methods to viral infections, which are rarely healing and some of the compensations contain the following:

Precise targeting of the viral particle with no metabolic opposing effects on the host. There are also many other important characteristics of the scheme of nano-viricides that are predictable to lead to minimalizing mutant generation.

- Nano-viricides are harmless because of their exclusive design and the detail that they are considered to be recyclable inside the body.
- The novel technology permits quick drug development in contradiction of an emerging virus, which would be significant for worldwide biosecurity in contradiction of usual as well as man-made conditions. It is thinkable to advance investigation drug in contradiction of a new dangerous viral disease inside 3-6 weeks after the contagion

is establish, i.e. as rapidly as an antibody from any animal foundation is accessible.

- The protection of nano-viricide medications is supported now as they specially violence the virus and not the host.
- A diversity of preparations, statement outlines, and directions of administration are probable.
- Low price of drug improvement, production, delivery.
- Advantages of Nano-viricides over vaccines are:
- Nano-viricides effort where vaccines do not work proper and are active even when the immune system is weakened such as in AIDS.
- Nano-viricides work where active vaccines are absent.
- Enough short-term defenses for a discrete outbreak collection.
- Management can be happening after infection.
- No essential to vaccinate whole world populace for controller of a viral rampant

Advantages of nanotechnology

Nanotechnology has the probable to carry main improvements in medicine. Nanobots could be referred into a patient's arteries to clear away obstructions (49). Surgeries could develop much faster and more correct. Damages could be mended cell-by-cell. It may even become probable to heal genetic disorders by fixing the injured genes. Nanotechnology could also be used to improve drug manufacture, modifying drugs at a molecular level to create them more active and decrease complications (50).

- A nanoparticle is drug distribution technique to brain for transferring drug particles through the blood–brain barrier (BBB) by using nanoparticles. These remedies cross the BBB and carry medications to the brain for therapeutic handling of neurological conditions.
- The benefits of using nanoparticles as a remedy transport system contain the following.
- Ordered and consistent drug discharge throughout transit and within the location, altering the medication's organ source, and subsequent confirmation of the therapy are all necessary for a full increase in efficacy of treatment and a reduction in side effects.
- Drug can be combined into the system without any chemical response; this is a significant influence for preservative the drug.
- Controlled discharge and drug degradation features can be readily controlled
- There is no waste of drug and thus improved bioavailability of remedy at precise site in right amount for lengthy epoch of time.
- It increases the solubility of unwell water-soluble remedies, extend half-life of drug complete movement by falling immunogenicity, relief drug at nonstop rate and minor the frequency of administration.
- It delivers relaxation and defiance to the patient and yet develops the therapeutic presentation of the drug over conventional arrangements.

CONCLUSION

Lately numerous differing logical procedures have been created for HCV treatment. Healing choices for HCV contamination have been constrained by calm barrier and unfavourable symptoms. A method for antiviral therapy that showed promise was concentrating on the replication of HCV. In any case, because of its immunosuppressive action and serious reactions, clinical applications in this class have been constrained. A standout amongst the most generally utilized delivery frameworks is nanoparticles of lipids. They are characterized by simplicity in creation and health, which facilitates them use it for in vivo RNAi. Lipid nanomaterials can also be synthesized and characterized to target specific cells and can be combined with conventional pharmaceutical components to increase effectiveness or lessen resistance. One of the one-of-a-kind points of interest of nanotechnology notwithstanding the productivity of medication delivery to obsessive regions is its capacity to diminish medications' poisonous quality and reactions. In this review, we discussed how a nanomaterials transport architecture might be secured and how it can serve as a Trojan horse for prospective therapies other than HCV.

SUMMARY

Ribavirin and interferon are used for many years for the treatment of HCV, direct acting agents and combination therapy as well. The main problem of these therapies is that a lot of side effects are there. Novel procedures are utilized for the treatment of HCV which is called nanotechnology. The major advantages of that technology are that there is no wastage of drug and avoid the hydrolysis of drugs. Different kinds of the bearer are utilized as a part of the treatment of HCV like nanoparticles, bio-

conjugation, micelle development and dendrites. Instead, then utilizing RBV alone, acylated polyglycerol adipate (PGA) NPs and polyglycerol adipate (PGA) NPs and were used to transfer RBV boronic destructive, which gives RBV hydrophobicity and increases the capacity of the NPs to assemble pharmaceuticals (51).

A nanoparticle is drug distribution technique to brain for transferring drug particles across the blood–brain barrier (BBB) by using nanoparticles (25). These remedies cross the BBB and carry medications to the brain for therapeutic handling of neurological conditions (52). Diverse sorts of Nano transporters are utilized that convey the medication stacked particles to target point and diminish symptoms. The role of nanoparticles (NPs) as a vehicle for anti-HCV vaccination, anti-HCV DNA enzymes, anti-HCV adjuvants, and anti-HCV phenolic chemicals and their targeted administration is discussed in this overview.

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