Clinical Trial to Evaluate and Compare the Therapeutic Efficacy of Coded Unani Drug UNIM–105 with Control Drug UNIM–106 in *Iltehab-e-Kabid Haad* (Acute Infective Hepatitis) Patients

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Abstract

Infective hepatitis (*Iltehab-e-Kabid Haad*) has been known chiefly as a sporadic, endemic and epidemic disease occurring in civilian populations all over the world. Infective hepatitis is the inflammation of the liver due to infection by viral and other agents. It is estimated that approximately 1.4 million persons die each year from various forms of viral hepatitis. No specific treatment is available for Infective viral hepatitis in conventional medicine. Supportive treatment including hospitalization is indicated for people with severe clinical manifestations. However, the drugs which are available are expensive and produce undue side effects. Many herbal preparations are claimed to be useful in the treatment of *Iltehab-e-kabid Haad* (infective hepatitis), however, no scientific data are available in support of these claims. The present study was undertaken to evaluate the therapeutic efficacy of coded Unani drug "UNIM-105" and to compare it with that of a standard drug "Ictrus (UNIM-106)" in patients of infective hepatitis. 165 cases in Group-I received the drug UNIM-105 and 133 cases in Group-II received the drug UNIM -106 in a dose of 1gm (2 capsules of 500mg in each group) orally thrice daily for a varying period of 30 and 40 days. The criteria of selection of cases for the study, the drug dosage, duration of treatment and follow-ups were uniform for both the groups. Age, gender and chronicity of disease wise distribution of patients were almost similar in both the groups. Subsidence of clinical sign & symptoms of Infective hepatitis was observed in patients after 10 days of treatment either with UNIM-105 or UNIM-106. Increased levels of serum bilirubin, SGOT &SGPT observed at base-line registered significant decline (< 0.001) towards normalcy during the course of treatment with UNIM-105 as well as with UNIM-106. Comparison of the results observed with drugs UNIM-105&UNIM-106 in the clinical study has revealed that the therapeutic efficacy exhibited by the drugs in terms of improvement in clinical as well as laboratory parameters were almost equal with no adverse effects.

Keywords: *Iltehab-e-Kabid Haad*, Infective hepatitis, UNIM-105, Ictrus.

Introduction

Iltehab-e-Kabid Haad is described in Unani system of medicine under the diseases of hepato biliary system and has been defined by ancient Unani Physicians as visible yellow or black discoloration of conjunctiva and skin due to diffusion of yellow or black bile in blood towards skin with or without putrefaction. The accumulation of vitiated matter due to continuous use of impure diet causes inflammation of liver (Khan, 1982; 2003; Multani, YNM; Razi, 2000; Samarqandi,

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2007). *Yerquan* (jaundice) is one of the main symptoms of Infective hepatitis (Azmi, 2000; Samarqandi, 2007).

Unani scholars have mentioned in their books that the texture of liver is quite susceptible to infections and diseased liver has severe impact on other body systems (Samarqandi 2007). Razi, has mentioned in his book "Al-Haawi" that the liver is full of narrow vessels and liable to get obstructed due to intake of thick or contaminated foods which leads to Warm-e-Kabid and infection (Razi, 2000). Hepatitis is a disease in which either the hepatic capsule, hepatic parenchyma or hepatic canaliculi gets inflamed (Ibn Sina, 1927; Kirmani, 1960), which is caused by injury, insects bite, congenital deformity, congestion and obstructions in the capillaries, excessive intake of meat, alcohol, oily and spicy foods, sweet preparations, certain drugs, improper diet and increased production of Safra (Khan, 2003).

Ibn Sina stated that the disturbed function of the liver is mainly due to its enlargement in the case of inflammation with swelling due to Waram Harr i.e. (Waram al-Kabid Damwi and Waram al-Kabid Safravi). Extensive inflammation which is located at the convexity of the liver is diagnosed by palpation and dry cough will be present. If inflammation is at the lower surface of the liver its diagnosis is made by secondary symptoms and palpation. Ibn Sina also stated that there are two main types of Yaraqan (jaundice). The first one is due to inflammation of the liver whereas the other is due to obstruction in the flow of bile. He pointed out that in all cases of Waram Harr, jaundice is present because of inflammation and obstruction in or vicinity of liver. Waram al-Kabid Had (Acute Hepatitis) also results from an inability on the part of Mirara (Gall Bladder) to properly absorb Khilt-e-Safra (Bile) and may lead to Yaraqan (Ibn sina, 1927; Khan, 2003; Razi, 2000).

Hepatitis is defined as an inflammation of liver and may be caused by a number of agents including viruses, bacteria and toxins. Acute hepatitis refers to an acute injury directed against hepatocytes. Hepatitis viruses A & E can cause acute hepatitis while hepatitis viruses B, C & D cause both acute as well as chronic hepatitis (Fauci *et al*., 2008; Hoslett *et al*., 1999; Juan Rodes, 2007; Kaplowitz, 1992; Munjal, 2012; Zuckerman, 1993). It is estimated that approximately 1.4 million persons die each year from various forms of viral hepatitis (Anonymous, 2012; Munjal, 2012).

Despite the incredible advancement in modern pharmacotherapy, there is no satisfactory treatment for hepatitis and with dearth of liver centric drugs in terms of safety, efficacy, remission of disease, and adverse effects which grossly suggests the need for development of formulations useful in the treatment of infective hepatitis (Thiagarajan 1990). Unani classical texts reveal the use of many Unani formulations in the treatment of infective hepatitis (Khan 2003; Razi, 1991, 2000),

however, no scientific data are available. UNIM–105 is a compound Unani herbo-mineral formulation possessing hepatoprotective, anti-inflammatory, deobstruent, diuretic and purgative properties and has ingredients that are beneficial in the treatment of hepatitis and related conditions (Anonymous, 2007; Anonymous, 2009; Razi, 1991). Hence the clinical study has been undertaken to evaluate the therapeutic efficacy of coded Unani drug UNIM–105 and to compare it with that of standard control drug Ictrus (UNIM–106) in infective hepatitis patients.

Material and Methods

Patients presenting with symptoms of infective hepatitis at the GOPD of the institute after careful history were subjected to thorough clinical examination for the diagnosis of Infective hepatitis and then to laboratory investigations for confirmation. Those cases fulfilling the criteria of selection viz; Patients of either gender in the age group of 12-65 years, with presence of clinical sign and symptoms of Infective hepatitis, presence of Bile pigment in urine and serum bilirubin level of 2-16 mg/dl were enrolled for the study after obtaining voluntary informed consent. Patients with history of systemic diseases such as diabetes, hypertension and pulmonary tuberculosis were not included in the study. Alcoholics, pregnant and lactating women were excluded from the study.

The clinical trial was approved by the Scientific Advisory Committee of C.C.R.U.M, New Delhi. The study was conducted at Regional Research Institute of Unani Medicine, Chennai over a period of five years in two stages.165 patients were enrolled for the study in the first stage in Group-I (Test group).133 patients were enrolled in Group –II (Control group)in the second stage. Patients in Group-I received drug UNIM-105 and in Group-II received UNIM-106 in a dose of 1 gm (two capsules of 500 mg in each group) orally thrice daily after food for a varying period of 30 - 40 days in IPD. The patients were advised rest and were allowed to take fat free diet throughout the course of treatment. No concomitant treatment for infective hepatitis was allowed during the entire trial period. Test drug UNIM-105 for the study was prepared at the pharmacy of the institute while control drug Ictrus (UNIM-106) was obtained from M/s Pharm products Pvt Ltd, Tanjore, T.N, India.

The patients were assessed for clinical progress and improvement in laboratory parameters on each follow-up at 10 days interval. The clinical assessment parameters were anorexia, dyspepsia, nausea, epigastric discomfort, yellow discoloration of conjunctiva, yellow discoloration of sub lingual surface and liver palpability. The pathological investigations included routine Haemogram, Urine examination for Bile salts, Bile pigment, Urobilinogen and Stool examination. Serum Bilirubin (Total & Direct), SGOT, SGPT, Alkaline Phosphatase, Total

Proteins, Albumin, Cholesterol, Glucose, Urea and Creatinine were the bio chemical investigations carried out. Blood and urine samples for investigations were collected at base line and on each follow-up. Standard procedures were used for the laboratory investigations. All the obtained data were subjected to statistical analysis for authentication of the study.

Results and Discussion

Table 1 depicts the age, gender and chronicity wise distribution of patients in Group -1 and Group – II. Out of 165 patients registered in Group-I (Test group), 122 cases completed the trial. In Group-II (Control group), out of 133 cases enrolled 107 cases completed the trial. 43 patients from test arm and 26 from control arm were lost to follow-ups due to personal reasons and due to non-compliance of the protocol guidelines (Table-2).

Table 1: Demographic data of *Iltehab-e-Kabid Haad* (IKH) (Infective Hepatitis) patients

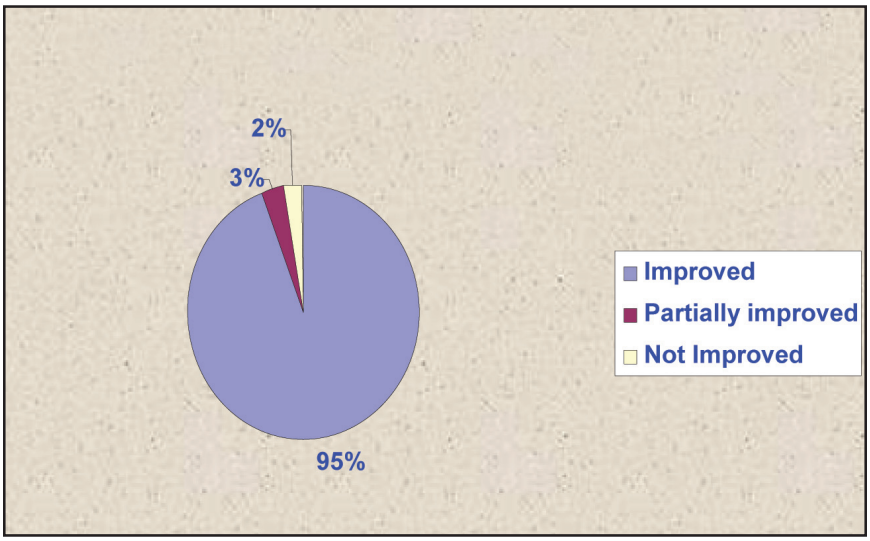
S.No.	Demographic data	Unit	Group–I (Test arm) n = 122	Group–II (Control arm) n = 107
1	Age	< 20 years	35(29%)	33 (31%)
		21-40	73 (60%)	59 (55%)
		41-60	14 (11%)	15 (14%)
		Mean ± SD	28.47±10.52	28.61±12.22
2	Gender	Male	93 (76%)	88 (82%)
		Female	29 (24%)	19 (18%)
3	Duration of disease (days)	< 20	97 (80%)	89 (83%)
		21-40	21 (17%)	16(15%)
		41-60	4 (3%)	2 (2%)
		Mean ± SD	14.65±11.29	13.14±10.49

Table 2: Details of *Iltehab-e-Kabid Haad* (Infective Hepatitis) patients registered & Response to treatment

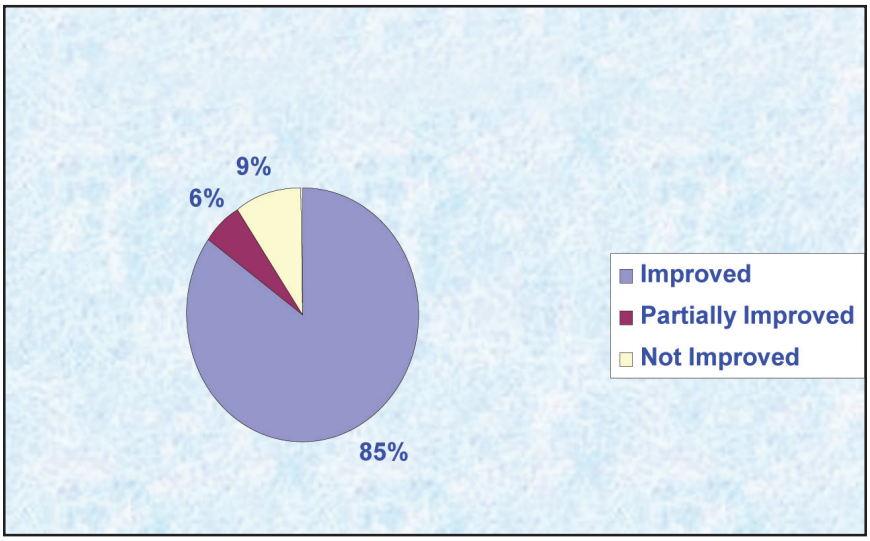
Drug	Total no. of cases enrolled	Dropout	Total no of Cases completed	Relieved	Partially Relieved	Not Relieved
UNIM-105	165	43	122	115 (94%)	4 (3.3%)	3 (2.5%)
UNIM-106	133	26	107	91 (85%)	6 (5.6%)	10 (9.3%)

Table 3: Response to duration of treatment in *Iltehab-e-Kabid Haad* (Infective Hepatitis) patients

Drug	Total no. of Cases Completed	Response & Duration of treatment					
		30 days			40 days		
		Relieved	Partial Relieved	Not Relieved	Relieved	Partial Relieved	Not Relieved
UNIM-105	122	103 (84%)	4 (3.3%)	—	12 (10%)	—	3 (2.5%)
UNIM-106	107	80 (75%)	4 (3.7%)	8 (7.4%)	11 (10%)	2 (1.9%)	2 (1.9%)



Graph 1: Overall response to treatment in IKH patients treated with coded drug UNIM-105



Graph 2: Overall response to treatment in IKH patients treated with coded drug UNIM-106

Out of 122 patients treated with UNIM-105 in test arm, 115 cases registered complete improvement in clinical and laboratory parameters. Improvement was observed in 30 days in 103 cases while 12 cases registered improvement in 40 days treatment. 4 cases showed partial improvement at the end of 30 days treatment, while 3 cases did not register improvement (Table – 3 & Graph- 1).

Out of 107 cases treated with UNIM-106 in control arm, 91 cases showed complete improvement in clinical, pathological and biochemical parameters of which 80 cases registered improvement in 30 days and 11 cases in 40 days treatment. 6 cases showed partial improvement while 10 cases did not show improvement (Table – 3 & Graph- 2).

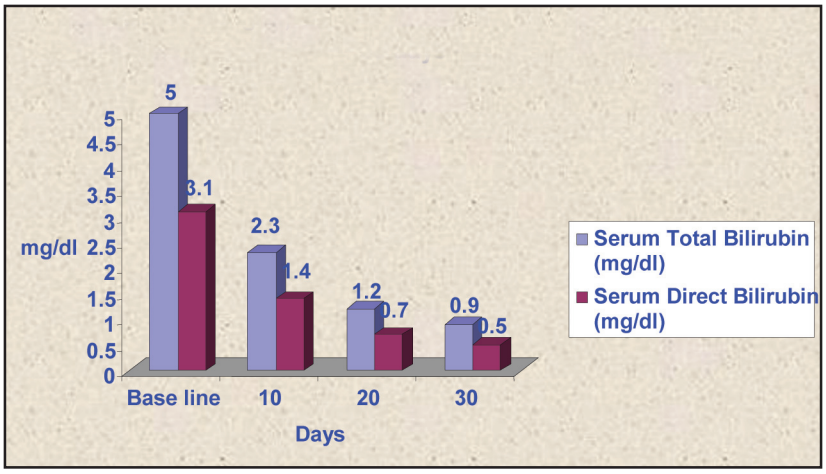
The efficacy of the trial drugs UNIM-105 & UNIM-106 was assessed on the basis of improvement observed in clinical and laboratory parameters and the response to treatment has been graded as Relieved, Partially Relieved and Not Relieved**.**

Relieved : When all the clinical sign and symptoms observed at base-line i.e. before treatment subsides and the biochemical parameters serum bilirubin, SGOT&SGPT return to normal/near normal levels, the patient is graded as relieved.

Partially Relieved : When majority of the clinical sign and symptoms observed at base-line i.e. before treatment subsides and the biochemical parameters serum bilirubin, SGOT & SGPT return towards normalcy but do not touch normal levels, the patient is considered to be partially relieved

Not Relieved : When there is no significant subjective improvement in the clinical condition of the patient and no improvement in the biochemical parameters, the patient is said to be not relieved.

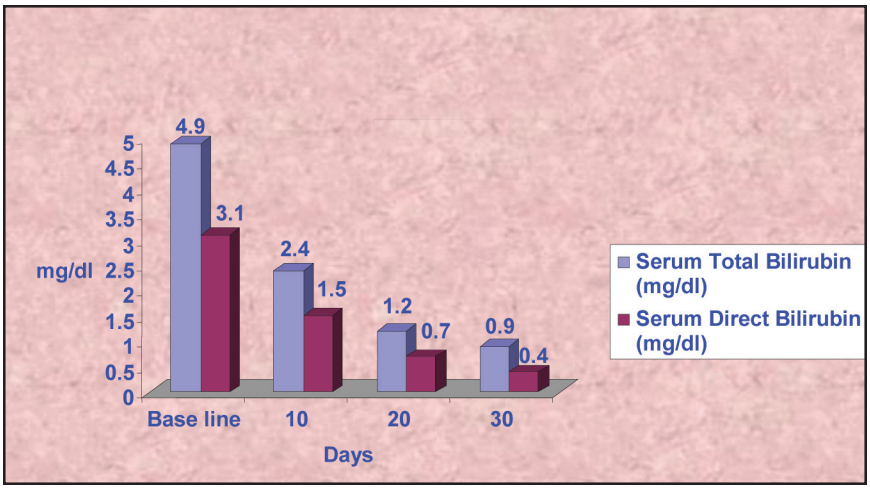
The improvement observed in clinical and laboratory parameters pertaining to relieved patients are depicted in tables 4 to 12 and graph 3 to10.



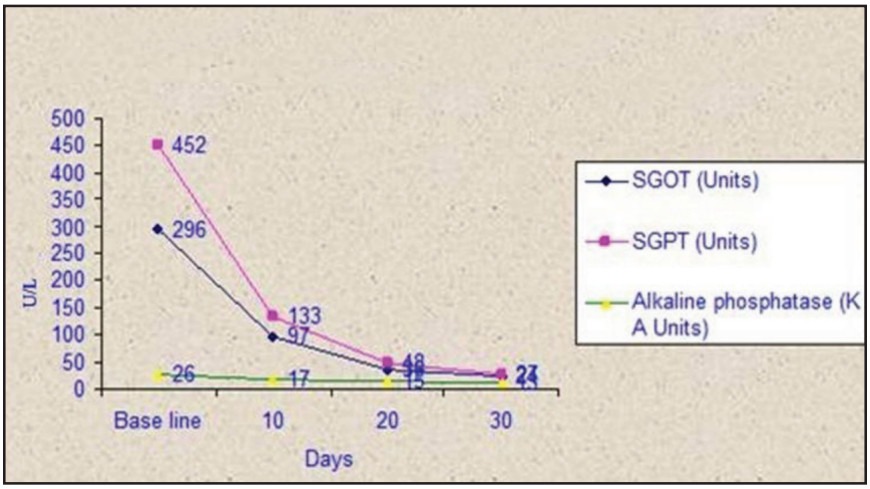
Graph 3: Serum Bilirubin levels in IKH patients (Base line serum bilirubin2- 8 mg/dl) treated with coded drug UNIM-105 for 30 days

Table 4: Clinical parameters in *Iltehab-e-Kabid Haad* (Infective Hepatitis) patients treated with UNIM-105 / UNIM – 106

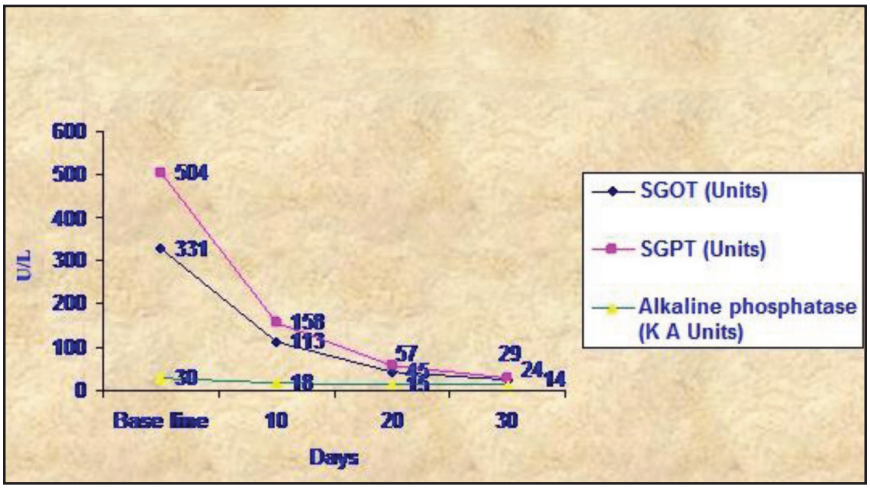
Sign & Symptoms		UNIM-105									UNIM-106								
		30 days n = 107				40 days n = 15					30 days n = 92				40 days n = 15				
		Base Line	After 10 Days	After 20 Days	After 30 Days	Base Line	After 10 Days	After 20 Days	After 30 Days	After 40 Days	Base Line	After 10 Days	After 20 Days	After 30 Days	Base Line	After 10 Days	After 20 Days	After 30 Days	After 40 Days
Anorexia	Present	103	3	1	—	15	3	1	1	—	87	3	1	1	15	—	—	—	-
	Absent	4	104	106	107	—	12	14	14	15	5	89	91	91	—	15	15	15	15
Dyspepsia	Present	89	1	—	—	13	1	1	1	—	73	1	2	2	5	—	—	—	—
	Absent	18	106	107	107	2	14	14	14	15	19	91	90	90	10	15	15	15	15
Nausea	Present	94	5	1	—	15	5	1	1	1	77	2	1	1	11	—	—	—	—
	Absent	13	102	106	107	—	10	14	14	14	15	90	91	91	4	15	15	15	15
Epigastric	Present	67	8	3	—	8	3	—	—	—	64	10	4	1	9	—	1	—	—
discomfort	Absent	40	99	104	107	7	12	15	15	15	28	82	88	91	6	15	14	15	15
Yellow	Present	107	83	33	1	15	15	13	9	—	92	84	41	9	15	14	14	7	3
discoloration of conjunctiva	Absent	—	24	74	106	—	—	2	6	15	—	8	51	83	—	1	1	8	12
Yellow	Present	107	79	27	2	15	15	14	7	—	92	82	35	8	15	14	11	6	4
discoloration of SLS	Absent	—	28	80	105	—	—	1	8	15	—	10	57	84	—	1	4	9	11
Liver palpability	Present	106	79	42	6	14	12	10	7	1	92	83	50	9	15	14	15	7	3
	Absent	1	28	65	101	1	3	5	8	14	—	9	42	83	—	1	—	8	12



Graph 4: Serum Bilirubin levels in IKH patients (Base line serum bilirubin 2- 8 mg/dl) treated with coded drug UNIM-106 for 30 days



Graph 5: SGOT & SGPT levels in patients (Base line serum bilirubin 2-8 mg/dl) treated with coded drug UNIM-105 for 30 days



Graph 6: SGOT & SGPT levels in IKH patients (Base line serum bilirubin 2-8 mg/dl) treated with coded drug UNIM-106 for 30 days

Table 5: Pathological parameters in *Iltehab-e-Kabid Haad* (Infective Hepatitis) patients treated with UNIM-105 / UNIM - 106

Parameters		UNIM-105									UNIM-106								
		30 days n = 107				40 days n = 15					30 days n = 92				40 days n = 15				
		BL	After 10 Days	After 20 Days	After 30 Days	BL	After 10 Days	After 20 Days	After 30 Days	After 40 Days	BL	After 10 Days	After 20 Days	After 30 Days	BL	After 10 Days	After 20 Days	After 30 Days	After 40 Days
Bile salts	Present	36	—	—	—	6	1	1	—	—	29	1	—	—	4	1	-	-	-
	Absent	71	107	107	107	9	14	14	15	15	63	91	92	92	11	14	15	15	15
Bile pigments	Present	107	22	2	—	15	13	10	5	3	92	33	11	8	15	11	6	1	-
	Absent	—	85	105	107	—	2	5	10	12	—	59	81	84	-	4	9	14	15
Urobilinogen	Increased	106	80	69	46	15	13	13	8	7	90	75	62	52	15	14	12	9	8
	Normal	1	27	38	61	—	2	2	7	8	2	17	30	40	-	1	3	6	7

Table 6: Showing improvement in Biochemical parameters in *Iltehab-e-Kabid Haad* (Infective Hepatitis) patients (Base line serum bilirubin 2-8mg/dl) treated with coded drug UNIM-105 / UNIM - 106 for 30 days

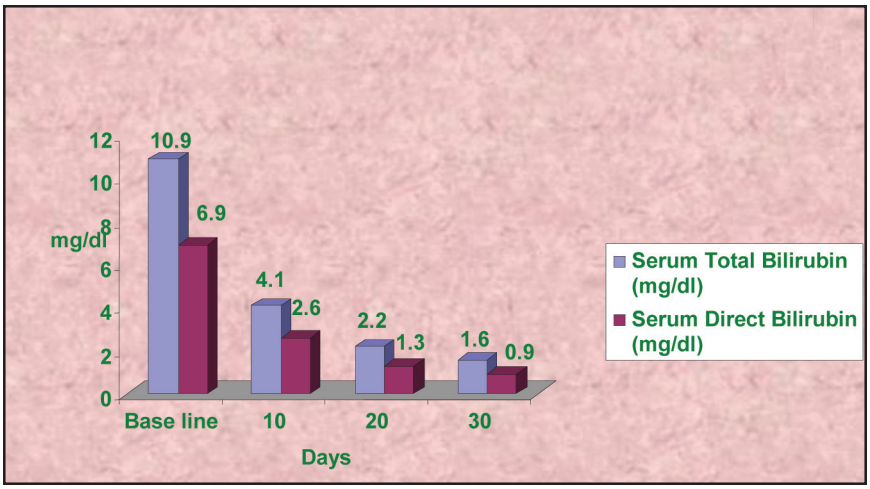
(Values are expressed as Mean ± S.D)

Parameters	UNIM – 105 n = 85				p value	UNIM – 106 n = 65				p value
	Base Line	After 10 days	After 20 days	After 30 days		Base Line	After 10 days	After 20 days	After 30 days	
Serum Total Bilirubin (mg/dl)	5.0 ± 1.68	2.3 ± 1.99	1.2 ± 0.65	0.9 ± 0.46	< 0.001	4.9 ± 1.5	2.4 ± 1.7	1.2 ± 0.7	0.9 ± 0.36	< 0.001
Serum Direct Bilirubin (mg/dl)	3.1 ± 1.19	1.4 ± 1.3	0.7 ± 0.42	0.5 ± 0.27	< 0.001	3.1 ± 1.09	1.5 ± 1.14	0.7 ± 0.52	0.4 ± 0.23	< 0.001
S.G.O.T (Units)	296 ± 152	97 ± 63	36 ± 32	24 ± 14	< 0.001	331 ± 120	113 ± 78	45 ± 48	24 ± 14	< 0.001
S.G.P.T (Units)	452 ± 244	133 ± 95	48 ± 47	27 ± 15	< 0.001	504 ± 198	158 ± 107	57 ± 68	29 ± 16	< 0.001
Alkaline phosphatase (K.A Units)	26 ± 12.2	17 ± 7.49	15 ± 5.4	13 ± 6.0	< 0.01	30 ± 13.6	18 ± 6.9	15 ± 6.3	14 ± 5.8	< 0.01

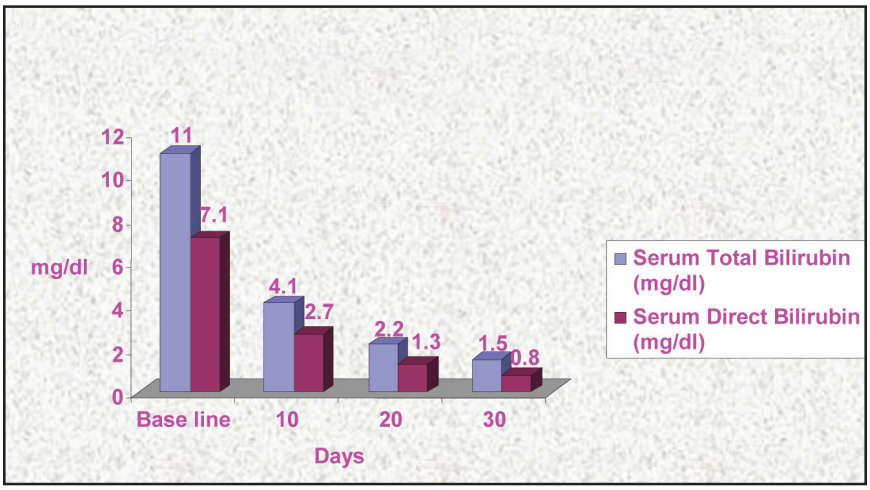
Within group: Z - test (Paired)

Table 7: Biochemical parameters in *Iltehab-e-Kabid Haad* patients (Bilirubin range 2-8 mg/dl) treated with UNIM-105/UNIM–106for 30 days

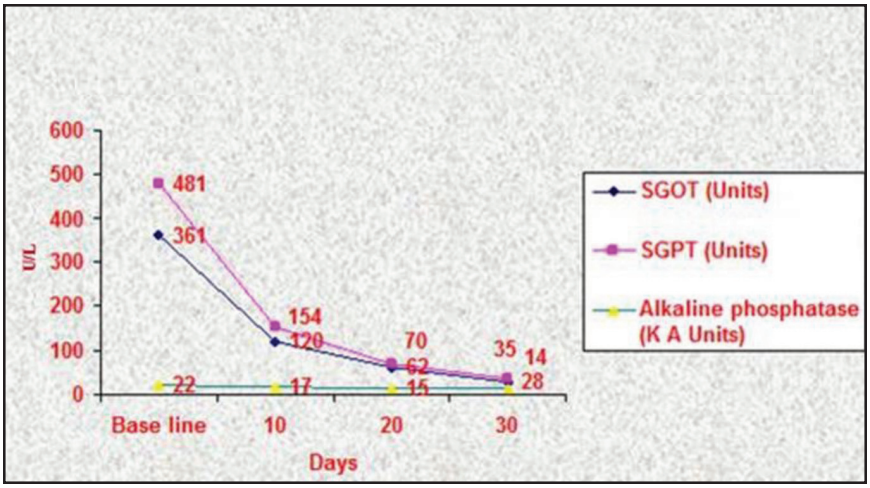
Bilirubin Range (mg/dl)	Parameters	UNIM – 105 (n = 85)				No. of cases	UNIM – 106 (n = 65)			
		BL	After 10 days	After 20 days	After 30 days		BL	After 10 days	After 20 days	After 30 days
2-4	S.T. Bilirubin-mg/dl	3.1±0.58	1.4±0.92	0.87±0.40	0.69±0.31	(n=26)	3.36±0.54	1.73±1.21	0.98±0.81	0.71±0.27
(n=30)	S.D. Bilirubin- mg/dl	1.84±0.46	0.79±0.59	0.4±0.24	0.3±0.18		2.09±0.53	1.03±0.87	0.56±0.57	0.35±0.16
	S.G.O.T (Units)	253±161	73±42	30±15	20±7		331±120	112±98	48±66	24±13
	S.G.P.T (Units)	367±249	97±62	38±22	25±9		490±207	146±131	60±95	28±15
	Alk.phosphatase-KA	22±9	16±6	14±5	13±4		34±16	20±9	16±8	14±7
4.1-6	S. T.Bilirubin-mg/dl	5.1±0.63	2.6±2.36	1.3±0.64	0.9±041	(n=24)	5.2±0.54	2.8±2.06	1.28±0.75	0.84±0.29
(n=30)	S. D.Bilirubin- mg/dl	3.2±0.58	1.6±1.60	0.75±0.45	0.49±0.26		3.3±0.46	1.74±1.34	0.73±0.47	0.42±0.19
	S.G.O.T (Units)	318±135	112±78	39±43	22±10		325±119	118±68	49±39	25±18
	S.G.P.T (Units)	493±220	156±122	50±63	25±13		499±182	168±98	62±48	31±19
	Alk.phosphatase-KA	25±13	16±8	14±6	11±4		26±11	17±5	13±4	14±5
6.1-8	S. T.Bilirubin-mg/dl	6.9±0.58	2.9±2.02	1.5±0.71	1.5±0.53	(n=15)	6.93±0.58	2.82±1.33	1.4±0.64	1.08±0.45
(n=25)	S. D.Bilirubin- mg/dl	4.5±0.50	1.7±1.35	0.8±0.46	0.5±0.30		4.56±0.56	1.78±1.01	0.86±0.46	0.6±0.31
	S.G.O.T (Units)	322±154	109±57	39±31	30±20		342±128	104±51	34±19	22±8
	S.G.P.T (Units)	506±246	149±81	55±50	32±22		554±212	139±71	43±28	26±7
	Alk.phosphatase-KA	31±13	18.6±9	15±6	15±9		30±12	17±4	16±6	13±5



Graph 7: Serum Bilirubin levels in IKH patients (Base line serum bilirubin 8.1 – 16 mg/dl) treated with coded drug UNIM-105 for 30 days



Graph 8: Serum Bilirubin levels in IKH patients (Base line serum bilirubin 8.1 – 16 mg/dl) treated with coded drug UNIM-106 for 30 days



Graph 9: SGOT & SGPT levels in patients (Base line serum bilirubin 8.1 - 16 mg/dl) treated with coded drug UNIM-105 for 30 days

Table 8: Showing improvement in Biochemical parameters in *Iltehab-e-Kabid Haad* (Infective Hepatitis) patients (Base line serum bilirubin 8.1-16mg/dl) treated with coded drug UNIM-105 / UNIM - 106 for 30 days

(Values are expressed as Mean ± S.D)

Parameters	UNIM – 105 (n = 18)				p value	UNIM – 106 (n = 15)				p value
	Base Line	After 10 days	After 20 days	After 30 days		Base Line	After 10 days	After 20 days	After 30 days	
Serum Total Bilirubin (mg/dl)	10.9 ± 2.34	4.1 ± 1.92	2.2 ± 0.61	1.6 ± 0.38	< 0.001	11.0 ± 1.87	4.1 ± 1.45	2.2 ± 0.69	1.5 ± 0.31	< 0.001
Serum Direct Bilirubin (mg/dl)	6.9 ± 1.86	2.6 ± 1.4	1.3 ± 0.35	0.9 ± 0.2	< 0.001	7.1 ± 1.32	2.7 ± 1.03	1.3 ± 0.49	0.8 ± 0.24	< 0.001
S.G.O.T (Units)	361 ± 210	120 ± 51	62 ± 44	28 ± 10	< 0.001	349 ± 141	133 ± 58	58 ± 42	39 ± 22	< 0.001
S.G.P.T (Units)	481 ± 244	154 ± 66	70 ± 48	35 ± 12	< 0.001	508 ± 250	184 ± 103	81 ± 69	46 ± 32	< 0.001
Alkaline phosphatase (K.A Units)	22 ± 12.3	17 ± 5.2	15 ± 5.4	14 ± 5.8	< 0.01	23 ± 5.6	17 ± 9.1	14 ± 5.5	15 ± 7.5	< 0.01

Within group: Student's t test (Paired)

Table 9: Biochemical parameters in *Iltehab-e-Kabid Haad* patients (Bilirubin range 8.1-16mg/dl) treated with UNIM-105/UNIM–106 for 30 days

Bilirubin Range (mg/dl)	Parameters	UNIM – 105 (n = 18)				No. of cases	UNIM – 106 (n = 15)			
		BL	After 10 days	After 20 days	After 30 days		BL	After 10 days	After 20 days	After 30 days
8.1-10 (n=8)	S.T.Bilirubin -mg/dl	8.76±0.57	3.86±1.36	2.25±0.62	1.5±0.23	(n=7)	9.65±0.13	3.82±1.45	2.05±0.64	1.47±0.37
	S. D.Bilirubin- mg/dl	7.3±2.06	2.5±1.10	1.3±0.30	0.93±0.15		6.34±0.22	2.37±1.08	1.28±0.56	0.8±0.31
	S.G.O.T (Units)	432±229	129±49	77±52	29±8		293±190	126±63	64±54	46±30
	S.G.P.T (Units)	542±237	165±55	88±61	33±11		510±321	182±101	84±80	49±37
	Alk.phosphatase-KA	26±15	19±6	16.5±6	18±5		23±5	18±13	15±7	18±11
10.1-12 (n=5)	S. T.Bilirubin -mg/dl	10.92	4.14	1.94	1.24	(n=6)	11.1±0.38	4.15±1.73	2.11±0.88	1.41±0.33
	S. D.Bilirubin- mg/dl	7.0	2.6	1.0	0.68		7.15±1.09	2.63±1.07	1.28±0.57	0.81±0.22
	S.G.O.T (Units)	235	96	41	31		424±70	143±68	61±37	34±16
	S.G.P.T (Units)	367	128	51	40		553±231	206±132	91±75	44±37
	Alk.phosphatase-KA	18	15	11	10		25±8	16±5	15±5	13±2
12.1-14 (n=2)	S. T.Bilirubin -mg/dl	13.55	6.2	2.4	1.9	—				
	S. D.Bilirubin- mg/dl	8.1	4.0	1.5	1.1					
	S.G.O.T (Units)	574	188	92	33					
	S.G.P.T (Units)	745	239	92	39					
	Alk.phosphatase-KA	29	21	22	18					
14.1-16 (n=3)	S. T.Bilirubin -mg/dl	14.66	3.16	2.33	1.96	(n=2)	15.15	5.15	2.7	1.5
	S. D.Bilirubin- mg/dl	4.93	1.5	1.13	0.88		9.65	3.65	1.5	0.85
	S.G.O.T (Units)	238	93	34	16		322	126	27	32
	S.G.P.T (Units)	330	115	39	26		367	124	40	38
	Alk.phosphatase-KA	15	11	11	9		19	14	12	12

Table 10: Showing improvement in Biochemical parameters *Iltehab-e-Kabid Haad* (Infective Hepatitis) patients (Base line serum bilirubin 2-8mg/dl) treated with coded drug UNIM-105 / UNIM - 106 for 40 days

(Values are expressed as Mean ± S.D)

Parameters	UNIM -105 n = 9						UNIM -106 n = 7					
	Base Line	After 10 days	After 20 days	After 30 days	After 40 days	p value	Base Line	After 10 days	After 20 days	After 30 days	After 40 days	p value
Serum Total Bilirubin (mg/dl)	5.5±1.82	7.2±4.23	4.8±2.19	1.9±0.69	1.2±0.29	< 0.001	4.7±1.69	4.9±2.93	2.3±1.60	1.60±0.95	0.9±0.35	< 0.001
Serum Direct Bilirubin (mg/dl)	3.6±1.39	4.6±2.79	3.2±1.54	1.2±0.48	0.7±0.17	< 0.001	3.1±1.25	3.2 ± 2.16	1.4 ± 1.09	1±0.69	0.5±0.23	< 0.001
S.G.O.T (Units)	304±146	292±114	197±98	93±59	33±17	< 0.001	434±183	257 ± 92	135±98	75±57	46±20	< 0.001
S.G.P.T (Units)	506±221	386±133	258±133	124±84	45±28	< 0.001	628±166	342±134	162±121	105±78	47±22	< 0.001
Alkaline phosphatase (K.A Units)	24±8.1	23±9.5	16±3.4	13±3.2	11.4±3.2	< 0.001	42±13.8	28 ± 12.7	25±9.3	23±11.8	20.4±12.1	< 0.001

Within group: Student's t test (Paired)

Table 11: Biochemical parameters in *Iltehab-e-Kabid Haad* patients (Bilirubin range 2-8 mg/dl) treated with UNIM-105/UNIM–106for 40 days

Bilirubin Range (mg/dl)	Parameters	UNIM – 105 (n = 9)					No. of cases	UNIM – 106 (n = 7)				
		Base Line	After 10 days	After 20 days	After 30 days	After 40 days		Base Line	After 10 days	After 20 days	After 30 days	After 40 days
2-4 (n=1)	S. T.Bilirubin-mg/dl	2.0	6.6	3.5	1.4	1.2	(n=3)	3.06	4.03	1.9	1.9	1.03
	S. D.Bilirubin- mg/dl	1.4	4.7	2.4	0.8	0.7		1.83	2.53	1.13	1.26	0.6
	S.G.O.T (Units)	439	428	226	36	25		523	299	183	119	65
	S.G.P.T (Units)	778	652	384	88	45		653	399	199	173	69
	Alk.phosphatase-KA	15	12	8	7	8		39	22	26	22	17
4.1-6 (n=5)	S. T.Bilirubin-mg/dl	4.9	8.0	4.4	1.7	1.14	(n=1)	4.1	1.4	0.8	0.8	0.7
	S. D.Bilirubin- mg/dl	3.1	4.86	2.82	1.08	0.6		2.6	0.7	0.3	0.4	0.3
	S.G.O.T (Units)	228	249	159	111	38		585	201	77	36	32
	S.G.P.T (Units)	407	370	211	146	56		746	235	123	39	30
	Alk.phosphatase-KA	22	24	17	13	10		69	56	44	50	49
6.1-8 (n=3)	S. T.Bilirubin-mg/dl	7.53	6.03	5.86	2.4	1.5	(n=3)	6.53	6.96	3.26	1.5	0.86
	S. D.Bilirubin- mg/dl	5.23	4.06	3.96	1.53	0.8		4.43	4.7	2.13	0.93	0.46
	S.G.O.T (Units)	388	318	249	69	28		295	234	106	44	32
	S.G.P.T (Units)	581	323	293	98	28		562	322	138	57	32
	Alk.phosphatase-KA	30	24	16	14	15		36	24	18	16	13

Table 12: Biochemical parameters in IKH patients (Bilirubin range 8.1-16 mg/dl) treated with UNIM-105/UNIM–106for 40 days

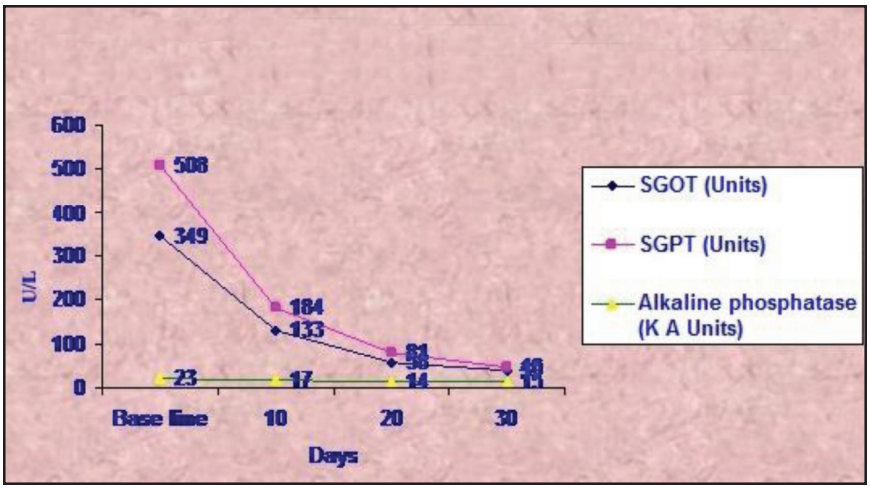
Bilirubin Range (mg/dl)	Parameters	UNIM – 105 (n = 3)					No. of cases	UNIM – 106 (n = 4)				
		BL	After 10 days	After 20 days	After 30 days	After 40 days		BL	After 10 days	After 20 days	After 30 days	After 40 days
8.1-10 (n=1)	S.T.Bilirubin-mg/dl	8.3	7.4	2.2	1.5	0.6	(n=2)	8.8	7.95	12	3.25	1.7
	S. D.Bilirubin- mg/dl	5.8	5.5	1.4	0.8	0.4		6.55	4.9	7.3	2.0	1.1
	S.G.O.T (Units)	540	286	141	28	30		394	250	213	92	29
	S.G.P.T (Units)	645	611	156	32	32		621	357	307	119	48
	Alk.phosphatase-KA	45	29	26	28	35		30	19	15	11	9
10.1-12 (n=1)	S. T.Bilirubin-mg/dl	10.9	8.8	2.9	1.9	1.0	(—)	-	-	-	-	-
	S. D.Bilirubin- mg/dl	7.5	6.2	1.9	1.2	0.6		-	-	-	-	-
	S.G.O.T (Units)	489	330	50	26	28		-	-	-	-	-
	S.G.P.T (Units)	804	410	81	29	29		-	-	-	-	-
	Alk.phosphatase-KA	51	29	25	28	15		-	-	-	-	-
12.1-14 (—)	S. T.Bilirubin-mg/dl	-	-	-	-	-	(n=1)	12.7	8.1	4.1	3.3	2.0
	S. D.Bilirubin- mg/dl	-	-	-	-	-		9.0	5.5	2.7	2.1	1.1
	S.G.O.T (Units)	-	-	-	-	-		121	177	164	68	12
	S.G.P.T (Units)	-	-	-	-	-		175	183	192	87	15
	Alk.phosphatase-KA	-	-	-	-	-		14	15	14	18	7
14.1-16 (n=1)	S. T.Bilirubin-mg/dl	14.9	9.4	6.2	2.6	1.5	(n=1)	15.8	16.6	5.9	3.2	1.7
	S. D.Bilirubin- mg/dl	9.3	6.2	4.0	1.6	0.8		9.7	10.8	3.5	2.1	1.0
	S.G.O.T (Units)	305	87	29	38	35		653	392	215	160	51
	S.G.P.T (Units)	341	130	29	40	51		969	657	296	211	57
	Alk.phosphatase-KA	20	24	11	18	18		38	23	16	9	10

Table 13: Showing Safety parameters in *Iltehab-e-Kabid Haad* (Infective Hepatitis) patients treated with coded drug UNIM-105 / UNIM - 106

(Values are expressed as Mean ± S.D)

Parameters	UNIM -105 n = 115			UNIM -106 n = 91		
	Base Line	After treatment	p value	Base Line	After treatment	p value
Serum Total proteins (g/dl)	6.6 ± 0.71	6.5 ± 0.64	> 0.05	7 ± 0.7	6.5 ± 0.6	> 0.05
Serum Albumin (g/dl)	3.5 ± 0.54	3.5 ± 0.48	> 0.05	3.4 ± 0.5	3.5 ± 0.5	> 0.05
B.Urea (mg/dl)	20 ± 7.71	17 ± 3.36	>0.05	20 ± 5.6	16.4 ± 3.2	>0.05
S. Creatinine (mg/dl)	0.8 ± 0.1	0.8 ± 0.04	> 0.05	0.8 ± 0.06	0.8 ± 0.06	> 0.05

Within group: Z - test (Paired)



Graph 10: SGOT & SGPT levels in IKH patients (Base line serum bilirubin 8.1–16 mg/dl) treated with coded drug UNIM-106 for 30 days

Clinical sign & symptoms observed at base-line subsided in majority of the cases after 10 days treatment (Table-4). Increased levels of serum bilirubin both in direct and indirect fractions, a manifold increase in SGOT and SGPT levels and moderate increase in Alkaline Phosphatase was observed at base line in patients of either groups treated with drug UNIM-105 /UNIM-106. Significant decline in the biochemical parameters towards normal range has been observed in majority of the cases during the course of trial either with UNIM-105 or UNIM-106 (Table – 6, 8 & 10).

Presence of Bile pigments observed in Urine in all the cases at base line became negative in majority of the cases during / at the end of trial (Table- 5).

The efficacy of the trial drugs was assessed on the basis of improvement observed in clinical and laboratory parameters. Accordingly 94% of the patients have been graded as relieved, 3.3% as partially relieved and 2.5% not relieved in case of treatment with UNIM-105 and 85% as relieved, 5.6% partially relieved and 9.3% not relieved in case of treatment with UNIM-106 (Table-3).

Discussion

Though Infective hepatitis is a self-limiting disease, it may go into severe form with prolonged course and serious complications (Fauci, 2008; Hoslett, 1999; Kaplowitz, 1992). The aim of the treatment is to reduce the course, prevent complications of the disease and is achieved through correction of inflammation of liver which is monitored by the assessment of the course of *Yerquan*. Lack of treatment for hepatitis in conventional medicine, unfavorable side effects with the anti-viral drugs necessitates the development of alternatives for the treatment and management of Infective hepatitis. Herbal preparations are claimed to be useful in the treatment of Infective hepatitis (Anonymous, 2007, 2009). UNIM-105 is a compound Unani formulation possessing ingredients that are useful in hepatitis and related conditions. The present study has been carried out to evaluate the therapeutic efficacy of the coded Unani drug UNIM-105 in patients of infective hepatitis and to compare it with that of standard control drug Ictrus (UNIM-106). The number of infective hepatitis patients studied, distribution of patients in terms of age, gender, chronicity of disease and serum bilirubin range were almost similar in both the groups. Majority of the patients in either drug groups were males in the age group of less than 40 years with mean age of 28.47 in test group & 28.61 in control group. The mean chronicity of disease was 14.65 days in UNIM-105 group while 13.14 days in UNIM-106 groups (Table-1). The base line serum bilirubin range was between 2-16 mg/dl.

For assessment of improvement in terms of biochemical parameters, the statistical analysis has been carried out in patients with base line serum bilirubin level 2-8 mg/dl and 8.1-16 mg/dl separately, which has helped in the evaluation of the efficacy of the drugs in patients with low as well as high serum bilirubin range. The student's't' test (paired) and 'Z' test (paired) were used for statistical analysis wherever necessary

Subsidence of clinical sign & symptoms of Infective hepatitis was noticed in majority of the patients in 10 days of treatment irrespective of the serum bilirubin range in both UNIM-105 & UNIM-106 groups. However improvement in biochemical parameters could be observed only after 20 days treatment. It may be noted from

tables 6 & 8 that the improvement observed in biochemical parameters was nearly 100% in 20 days treatment in patients with base-line serum bilirubin range 2-8 mg/dl, whereas in the patients with base-line serum bilirubin range 8.1-16 mg/dl, 100% improvement was observed only after 30 days treatment either with UNIM-105 or UNIM-106 suggesting that the improvement observed was quicker in patients with low serum bilirubin range when compared to patients with higher bilirubin levels. Analysis of results observed in UNIM -105 /UNIM-106 Groups with class interval of 2 mg serum bilirubin also revealed the same as evident from tables - 7, 9, 11 & 12.

It may be observed from table - 6 that significant reduction in serum bilirubin from 5.0 ± 1.68 to 0.9 ± 0.46, SGOT from 296 ± 152 to 24 ± 14, SGPT from 452 ± 244 to 27 ± 15 was observed in 30 days treatment in UNIM- 105 group. The magnitude of reduction in serum bilirubin, SGOT and SGPT in 30days treatment were almost same in UNIM-106 group i.e. serum bilirubin has declined from 4.9 ± 1.5 to 0.9 ± 0.36, SGOT from 331 ± 120 to 24 ± 14, SGPT from 504 ± 198 to 29 ± 16.

The same status of reduction in serum bilirubin, SGOT and SGPT was noticed in patients with base-line serum bilirubin range 8.1-16 mg/dl during the course of treatment either with UNIM-105 or UNIM-106 as evident from table - 8. The significant fall observed in SGOT & SGPT, appreciable decline noticed in serum bilirubin levels with either UNIM-105 or with UNIM-106 treatment suggests the arrest of cellular necrosis and inflammation during the course of treatment (Fauci, 2008; Kaplowitz, 1992).

94% of the patients in UNIM-105 group and 85% of the patients in UNIM-106 group registered complete improvement. The total recovery as evident by the normalization of clinical and laboratory parameters took more or less same duration in UNIM -105 as well as in UNIM-106 drug group i.e. 30 days treatment in majority of the cases and 40 days treatment in few cases (Table - 10) indicating that treatment with UNIM-105 as well as UNIM-106 has restored normal liver function, clearing jaundice and improving clinical symptoms thereby suggesting that the therapeutic efficacy of UNIM-105 & UNIM-106 are almost equal and comparable.

The exact mechanism of protective effect of UNIM-105 is not known. However it may be attributed to its multipronged action due to its ingredients possessing hepatoprotective, anti-inflammatory, deobstruent, diuretic and purgative properties as widely reported in the classical texts (Anonymous, 2007; Anonymous, 2009; Razi, 1991; Razi, 2000) and in some scientific studies (Gupta *et al.*, 2013; Tahir *et al.,* 2009; Ahmed, 2013; Naseem, 2009; Sultana *et al.*, 1995). Further expulsion of the morbid *Safravi* humour and restoration of normal hepatic functions as evident from the subsidence of clinical sign and symptoms of IKH and normalization of laboratory parameters may also be attributed to the multipronged action.

Serum total proteins and albumin levels were well within the normal range in both UNIM-105 & UNIM-106 drug groups suggesting that the cases studied were in the acute phase of illness. Maintenance in the protein and albumin levels suggests that none of the cases treated either with UNIM-105 or UNIM-106 has gone in to chronic stage. The maintenance of urea and creatinine levels throughout the course of treatment either with UNIM-105 or UNIM-106 suggests that there is no nephro toxic side effect due to drug intervention (Table – 13).

Conclusion

The magnitude of improvement observed in clinical, pathological and biochemical parameters of the Infective hepatitis cases treated either with UNIM-105 or with UNIM-106 were almost same. The efficacy observed and non-toxic nature of these drugs suggests the utility of these formulations in the management of *Iltehab-e-kabid had* (Infective Hepatitis). The study also revealed that the therapeutic efficacy exhibited by UNIM-105 and UNIM-106 are almost equal and rationally comparable.

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