Redesigning of the Unani Preparation from Powder Form into Tablet and its Standardization Along with HPLC Profile

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Abstract

Tablet is one of the most suitable and preferred solid dosage form used all over the world. Almost all drug molecules can be formulated as a tablet and the process of manufacturing of tablets is very simple, and flexible. One can administer 0.01 mg to 1 gm of a drug as a tablet by the oral route. Therefore, in the present study an anti-arthritic pharmacopoeial preparation in powder form having ingredients Suranjan Talkh(*Colchicum luteum*), Zanjabeel Khushk (*Zingiber officinale*) and Elwa (*Aloe vera*) were re-designed and modified for use in the form of Tablet (Qurs) and standardized. Organoleptic characters of tablet, tests for weight variation, uniformity of diameter and thickness, hardness, disintegration time and friability of tablets were conducted for standardization and the values obtained indicated the compliance with the pharmaceutical standards. HPLC profile of tablet and qualitative analysis of chemical constituents present in the tablet were also determined. Furthermore, tablets were also tested for the presence of pesticidal residue by comparing HPLC profile of pesticides and tablet in identical conditions and the result shown absence of pesticides in the formulation. These tablets can be used as an alternative of powder form of the given formulation and the findings will help to set the standards for future reference.

Keywords: Re-design, *Colchicum luteum, Zingiber officinale, Aloe vera,* Tablet, and HPLC

Introduction

The Unani System of Medicine and its pharmaceutics are most suitable to the people of the Indian subcontinent as it was not only the part of culture and heritage but has a long cherished history during the ages of different dynasties and reigns. But in this scientific era fast paced life style emerged with exploration of various scientific inventions in the biomedical fields and pharmaceutical sciences in accordance with the need and requirement of the modern age. The pharmaceutical industries of traditional and herbal medicine came up with the invention of convenient dosage form development in accordance with the demand of biomedical requirements as well as to provide better compliance to the patient.

Tablet is one of the most convenient and appropriate solid dosage form provided an accurately measured dose in a convenient portable package; and can be designed to protect unstable medications or disguise unpalatable ingredients. Tablets are most stable of all oral dosage forms and easy to swallow. They are very economical also (http://tabletsdosageform).

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Therefore, in view of above and in order to achieve global acceptance, a modification has been made to pharmacopoeial Unani formulation mentioned in "Ilaj al Amaraz" (Khan, 1870) i.e. from powder form in to the tablet as most of the dosage forms falls in this category, by adding Gum Acacia (S. d. Fine Chemical Ltd.) as an excipient along with its standardization which can also provide the better compliance to the patient. Further, one of the ingredients of the formulation that is Aloe is extremely bitter in taste and the consumption of the drug per oral in powder form would be more distasteful to the patient which can be easily used in the form of tablet. Parameters for tablet standerdisation include organoleptic characters, physical parameters, qualitative analysis and HPLC profile of tablet. In the form of tablet the formulation seems convenient to take and easy to handle by the practitioners and patients. The dosage of the formulation becomes more specific and accurate in the form of the tablet.

Ingredients of formulation

(1) Sonth (*Zingiber officinale* Linn. – Dried Rhizome)	3.5 g
(2) Suranjan talkh (*Colchicum luteum* Baker – Dried Corm)	3.5 g
(3) Elwa (*Aloe vera* Linn. – Dried Exudate)	7.0 g

Material and Methods

Crude drug collection and authentication

The raw materials were procured from the local market of Aligarh and the samples were authenticated in pharmacognosy section of the department of Ilmul Advia, Faculty of Unani Medicine by Prof. S. H. Afaq and found within range of standards as mentioned in Ayurvedic and Unani Pharmacopoeia of India (Anonymous, 1999, 2001 and 2007).

Preparation of tablet

The two ingredients of formulation 'Sonth' and 'Suranjan talkh' were powdered in an electric grinder and Elwa was made Mushawwa (broiled or roasted) by keeping in an Apple, covered it by the process of Kapoorti, and heated in an oven, till it was brown. Now, Elwa was taken out of apple and dissolved in distilled water as required, after few minutes it was filtered and then concentrated. All the three ingredients were mixed together in order to make Lubdi (dough). The mixture was dried in shed and then powdered in a mortar. This powder was mixed with a suitable inert substance viz. powder of Gum Acacia (S.d. Fine Chemical Ltd.) as excipient. The material in the requisite degree of fineness mixed and damped with a moistening agent (purified water). The moistened material was made into granules by passing through a sieve. The granules were dried in shed and again

passed through a sieve for uniformity of size. Tablets of 500 mg were made by Automatic tablet making machine in Dawakhana Tibbiya College, AMU, Aligarh (Anonymous, 1968; 1970).

Standardization of the tablet dosage form

The tablets were evaluated for various quality control parameters like organoleptic characters (appearance, color, smell, taste and texture), weight variation, diameter, thickness, hardness, friability and disintegration time. Qualitative analysis and HPLC profile of tablet was also done. Tablets were also tested for the presence of pesticides by comparing the HPLC profile of tablet with the HPLC of standard samples of pesticides.

Organoleptic characters

Twenty tablets were taken to check for appearance and any discoloration or degradation, if any, by visual method (Patel *et al.,* 2010). Tablets were also tested for their smell, taste and texture. All the data obtained were based on random selection and multiple observations.

Weight variation of tablet

Ten tablets were selected randomly and weighed individually by an Electronic weighing machine to check for weight variation and was expressed in mg. Weight ± 5% deviation is acceptable for the tablets / pills having average weight 250mg or more, hence considered as appropriate (Subrahmanyam *et al.,* 2006; Dandagi *et al*., 2006).

Diameter of tablet

Uniformity of Diameter was assessed by picking three tablets randomly and the diameter was measured individually by using a Digital Vernier Caliper and expressed in mm. (Subrahmanyam *et al.,* 2006; Dandagi *et al*., 2006).

Thickness of tablet

Uniformity of Thickness was assessed by picking three tablets randomly and the Thickness was measured individually by using a Digital Vernier Caliper and expressed in mm. (Subrahmanyam *et al.,* 2006; Dandagi *et al*., 2006).

Hardness of tablet

Hardness or Tablet crushing strength (the force required to break a tablet in a diametric compression) was measured using Monsanto Tablet Hardness Tester and expressed in kg/cm^2 (Subrahmanyam *et al.,* 2006; Vijaya and Mishra, 2006).

Determination of disintegrating time

The rate of disintegration was measured by a Disintegration-Testing Apparatus using the two media, the aqueous and the acidic and expressed in minutes. For measurement in aqueous medium double distilled water was taken and for measuring in acidic medium simulated gastric fluid (pH about 1.2) was prepared without enzyme by dissolving 1gm of NaCl in 500 ml of distilled water, adding 7 ml of concentrated HCl, and diluting the volume to 1000 ml with water (Subrahmanyam *et al.,* 2006; Anonymous, 1989) and modified by Afaq *et al.* (1994).

Friability test

Friability is the loss of weight of tablet in the container / package, due to removal of fine particles from the surface. Friability of tablets was determined by using Roche Friabilator and expressed in percentage (%). This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablet at a height of 6 inches in each revolution. Pre weighed sample of tablets were placed in the friabilator and were subjected to 100 revolutions. Tablets were de-dusted using a soft muslin cloth and re-weighed. The friability (*f*) is calculated by the following formula.

$$f = \left(1 - \frac{W_0}{W}\right) \text{x} 100$$

Where, W_0 is the weight of the tablets after the test and W is the weight of the tablets before the test (Subrahmanyam *et al.,* 2006; Vijaya and Mishra, 2006).

Qualitative analysis of chemical constituents

The qualitative analysis of different chemical constituents, present in the tablet was carried out according to the scheme proposed by Bhattacharjee and Das (1969). This scheme has been given in the form of Flow Chart (Fig. 1).

The powder of compound formulation was extracted with petroleum ether. The petroleum ether extract (I) was tested for free phenols, alkaloids and sterols/ terpenes. A part of this extract was saponified and sap portion (II) was tested for fatty acids, whereas, unsaponified portion (III) was tested again for alkaloids, phenols, and sterols/terpenes for confirmation. The defatted marc was divided into two portions. One portion was extracted with hot water and the other with ethanol (70%). The aqueous (IV) and ethanolic (V) extracts were tested for alkaloids, flavonoids, saponins, sugars and tannins. Aqueous extract was extracted with ether and ether soluble portion (VI) was tested again for alkaloids, sterols/ terpenes, whereas, water-soluble portion (VII) was tested for glycosides. The water-soluble portion was again hydrolyzed with 5% hydrochloric acid and extracted

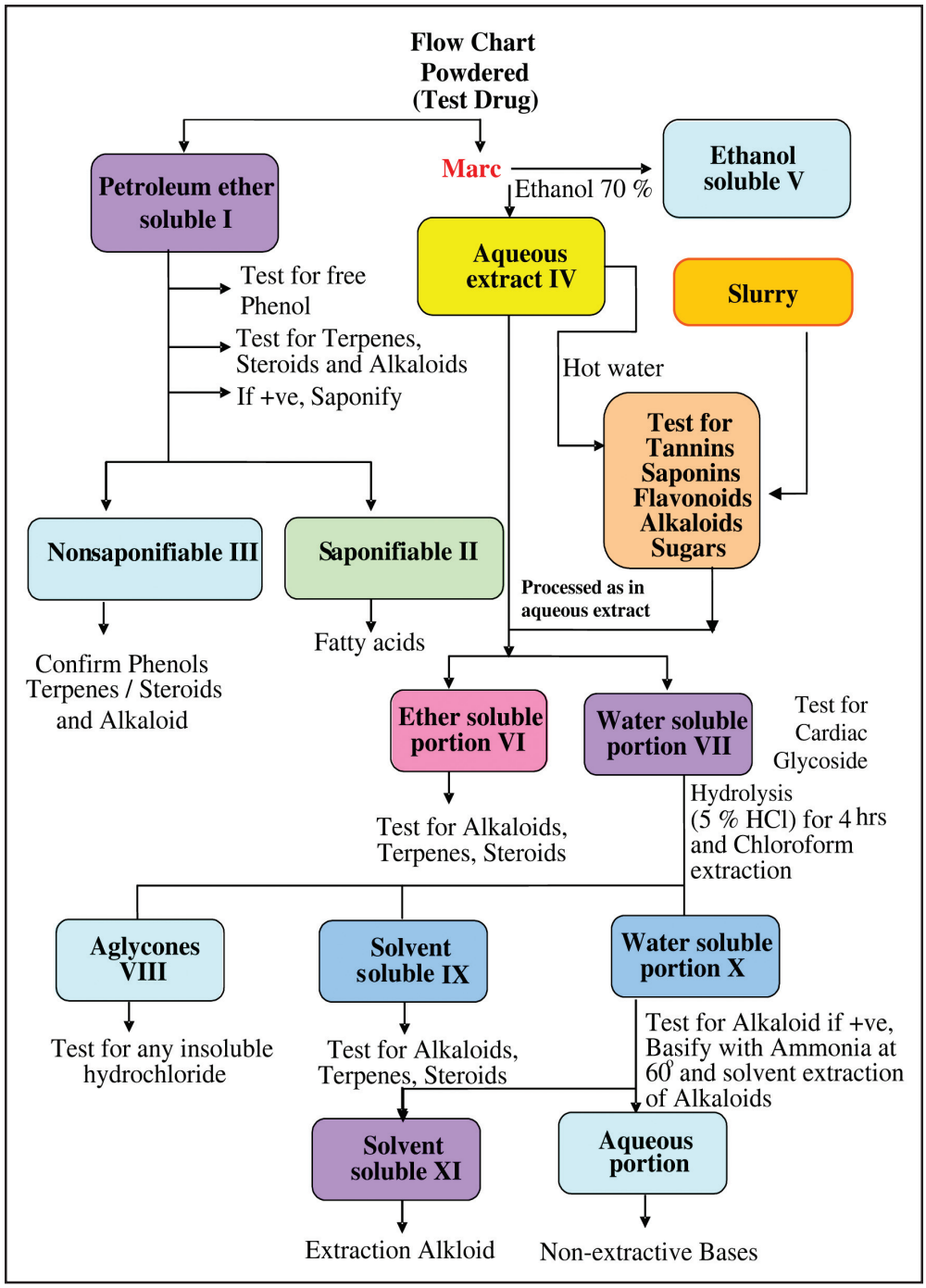

Fig. 1: Scheme for qualitative analysis of chemical constituents in the tablet

with chloroform. The aglycone portion (VIII) was tested for insoluble hydrochloride of alkaloid. Chloroform soluble portion (IX) was tested for alkaloids and sterols/ terpenes, whereas; water-soluble fraction (X) was tested for alkaloids. One part of this water-soluble portion was basified with any alkali (ammonia) and extracted with immiscible solvent (ether). The solvent soluble part (XI) was again tested for alkaloids.

Qualitative chemical analysis of the tablet for above mentioned compounds were carried out by different tests and methods for the determination of the presence of active compounds (Overtone, 1963; Harborne, 1973 and Afaq *et al.*, 1994).

HPLC profile of the tablet

General HPLC profile of the hydroalcoholic extract of the tablet was done by a Cyber lab's HPLC system equipped with a single pump and porous silica with 5 ìm diameter, C 18 4.6×250 mm column and software driven peaks were obtained. The pressure, temperature and flow rate was 7 Pa, 25^0C and 1.0 ml/min, respectively. Detector for HPLC was UV and the wave length was 254 nm. Mobile phase for HPLC profile of extract consisted of acetonitrile: water (55:45). The hydroalcoholic extract of coarsely powdered drug was determined with the help of Soxhlet's apparatus for 6 hours, extract was filtered and allowed to evaporate on water bath. 20mg of hydroalcoholic extract was dissolved in 1ml of HPLC grade distilled water and used for study.

Determination of Pesticidal residue

Common pesticides (Chloropyriphos, DDT, Parathion, Malathion and Endosulphan) were obtained from Sigma-Aldrich, mixed properly and dissolved in Acitonitrile. This standard was injected in the C18 column of HPLC instrument (Cyber lab, USA) considering the retention time in the identical conditions as in the HPLC profile of the test drug and software driven peaks were obtained. These peaks were compared with the peaks of tablet.

Results and Discussion

Organoleptic characters are the first step to identify the drugs and also indicate the status and condition of the drug. If any discoloration or black spots appears, it shows the degradation or decomposition of the in the tablet (Patel *et al,* 2010). Organoleptic properties like colour, taste, smell, appearance and texture were noted and depicted in Table 1.

Table 1: Organoleptic description of formulation tablet

Appearance	**Tablet**
Colour	Dark Brown
Smell	Agreeable
Taste	Pungent
Texture	Hard

A good quality tablet should be accurate and uniform in weight, diameter and thickness. But diameter and thickness of a tablet can vary without any change in its weight. Tablet's diameter and thickness are controlled by the machine tooling, includes a die and punch. This is called a station of tooling. The thickness is determined by the amount of tablet material and the position of the punches in relation to each other during compression (http://en.wikipedia.org/wiki/Tablet). It should be controlled within a ±5% variation of standard value (http://www.pharmainfo.net/namanm/evaluation-tablets). The uniformity of weight, diameter and thickness was found to be within the prescribed limit and mean values are shown in Table 2.

Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shakes during manufacture, packaging, shipping and handling by the pharmacist and patient. The resistance of the tablet to chipping, abrasion or breakage under above mentioned condition before usage depends on its hardness and friability. Hardness and Friability loss indicate that tablets have good mechanical resistance and have ability to with stand abrasions. A loss less than 1% is considered acceptable by industrial standard and all the tablets were found well within approved range to give good handling properties without breakage or excessive friability problems.

Tablet should be hard enough to withstand manufacturing, packaging, and transportation process. However they cannot be too hard since that may alter disintegration or release of the drug product. Disintegration roughly indicates the possible pattern of dissolution of active substance. Hence, the experimental conditions closely mimic the situations that a tablet encounters in gastrointestinal tract, in terms of temperature, pH and mechanics. Physical parameters such as area, hardness, surface characteristics and size can significantly affect the rate of disintegration of drugs contained in a complex system. After administration,

Table 2 : Parameters for standardization of tablet

S.No.	Parameters	Result (Mean±SE)
1.	Weight variation of Formulation Tablet (g)	0.525 ±0.01
2.	Uniformity of Diameter (mm)	13.54 ± 0.00
3.	Uniformity of Thickness (mm)	4.77 ± 0.01
4.	Hardness (kg/cm^2)	2.67 ± 0.17
5.	Friability (%)	0.47 ± 0.01
6.	Disintegration time in the water (minutes)	12.17 ± 0.39
7.	Disintegration time in the simulated gastric fluid (minutes)	10.14± 0.52

the tablet should disintegrate readily for quick absorption in gastro-intestinal tract; therefore, the tablets were also subjected for the evaluation of Disintegration time. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass. It is mentioned that uncoated tablets must disintegrate in not more than 45 minutes (Anonymous, 1989). Results for hardness, friability loss and disintegration time illustrated in Table 2.

The therapeutic properties of the crude drugs are mainly due to presence of physiologically active chemical constituents present in the drugs. The presence and absence of active compounds are shown in Table 3.

HPLC Analysis

The HPLC profile of the formulation was recorded as the obtained graph can be compared with the batches in future. The HPLC pattern shows 15 peaks and the peak no. 1 is major peak having concentration 84.632% and retention time was found to be 1.98 min. The details are depicted in Fig. 2 and Table 4. HPLC is an important qualitative and quantitative analytical procedure. By doing HPLC we can also determine the impurities in the formulation. If there is any change in no. of peaks or retention time or area of peaks from standard it indicates adulteration or deterioration in the drug. The HPLC profile of the mixture of different pesticides

Table 3: Qualitative analysis of chemical constituents

S.No.	Tested for	Result
1.	Alkaloids	+ ve
2.	Amino acids	- ve
3.	Fixed oil / Volatile Oil	+ ve
4.	Flavonoids	+ ve
5.	Glycosides	+ ve
6.	Phenols	+ ve
7.	Proteins	- ve
8.	Resins	- ve
9.	Saponins	+ ve
10.	Sterols / Terpenes	+ ve
11.	Sugar (Reducing)	- ve
12.	Sugars (Non-reducing)	- ve
13.	Tannins	+ ve

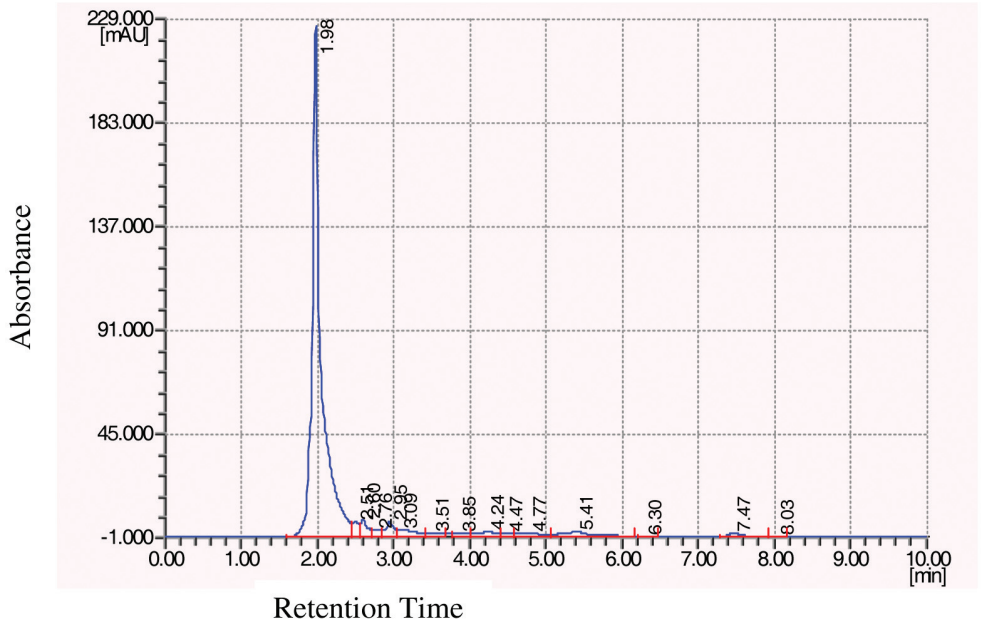

Fig 2: HPLC Profile of the Tablet

Table 4: HPLC Profile of the Tablet

ID	Name	Retain.T	Height	Area	Conc	Tail. Factor	Theo. Plate
1		1.908	22622	185305.8	84,632	1.43	1165
2		2.509	678	3404.8	2.536	1.00	4974
3		2.600	782	4709.3	2.926	2.00	3716
4		2.758	334	2141.5	1.250	1.89	3689
5		2.950	679	4883.2	2.540	1.00	3354
6		3.092	332	5293.5	1.242	4.54	749
7		3.512	167	2262.3	0.625	1.50	1339
8		3,853	145	1907.9	0.542	1.62	1709
9		4.236	245	3758.5	0.917	0.90	1520
10		4.473	138	1264.5	0.516	1.38	4750
11		4,773	177	3669.7	0.662	1.28	1056
12		5,407	234	5956.6	0.875	1.64	890
13		6,302	14	127.0	0.052	1.35	9616
14		7,472	171	1821.3	0.640	1.41	9808
15		8.025	12	93.6	0.045	1.07	21100
	Sum:		26730	226599.8	100.0000		

in Acetonitrile depicted in Fig. 3 and table 5, shows there is no any peak corresponds to the HPLC profile of tablet indicating absence of pesticides in the test drug. A comparison of both of them is also shown in Fig. 4.

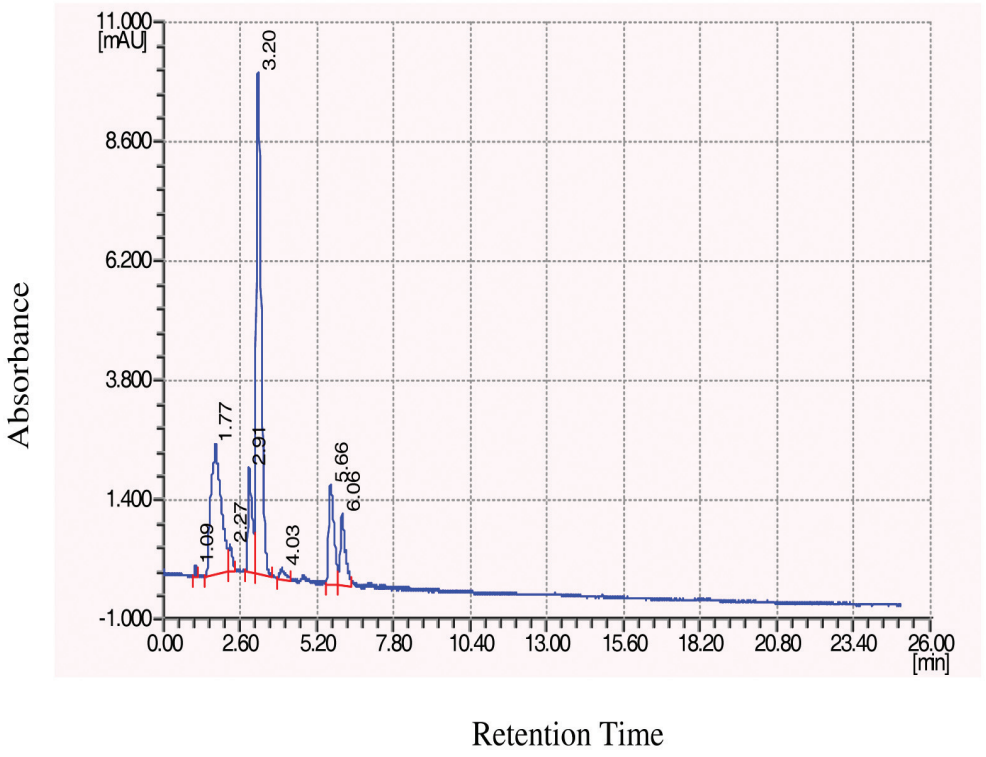

Fig 3: HPLC Profile of the mixed pesticides

Table 5: HPLC Profile of the Tablet

ID	Name	Retain.T	Height	Area	Conc	Tail. Factor	Theo. Plate
1		1.092	23	82.9	1.197	1.19	1830
2		1,768	261	6405.7	13.580	1.24	103
3		2.268	54	378.2	2.810	2.25	2091
4		2.912	210	2042.2	10.926	1.12	1787
5		3,203	1009	11936.6	52.497	2.02	1461
6		4.030	21	294.6	1.093	1.22	1645
7		5.665	199	2523.1	10.354	1.27	3979
8		6.058	145	1701.5	7.544	1.73	5313
	Sum:		1922	25364.7	100.0000		

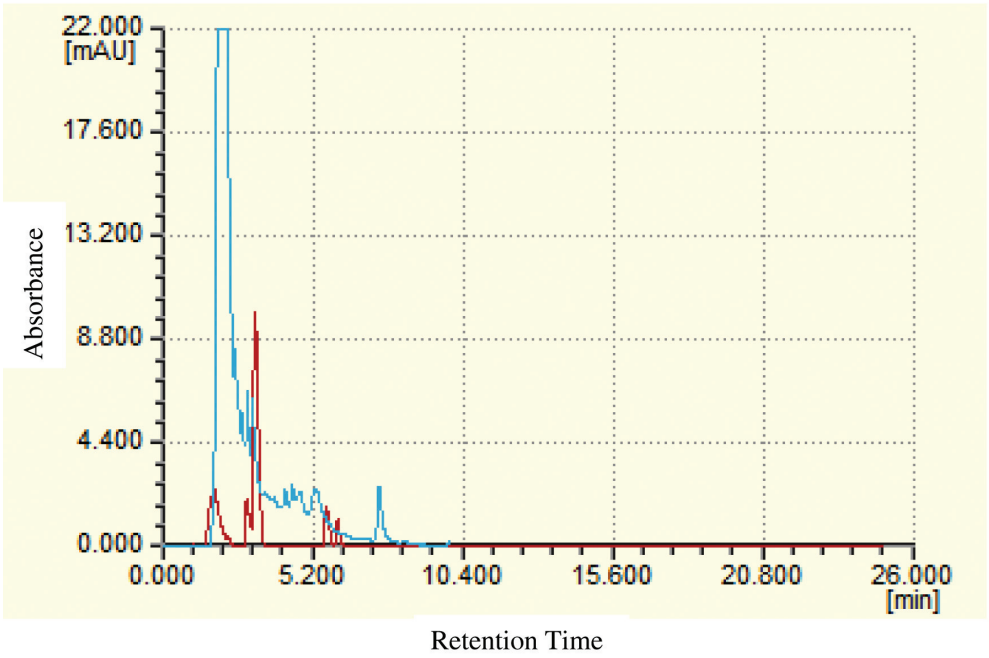

Fig 4: Comparison of HPLC profile of tablet and mixture of pesticides (Peaks with sky blue and red colour indicates HPLC profile of tablet and pesticides respectively)

Conclusion

This study assumes great significance as it will provide a key of diagnostic characters specially HPLC profile which serves as an important tool in laying down the standards for quality assurance. The parameters applied for standardization of formulation viz. organoleptic characters, friability and HPLC etc. may be taken as standard parameters for future reference.

The study also offers an improvement in Unani health care system by redesigning of powder (Safoof) form which is less convenient to use into the more convenient tablet form.

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