Standardization and Quality Control Parameters Required for Unani Medicines

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STANDARDIZATION AND QUALITY CONTROL PARAMETERS FOR UNANI MEDICINES

INTRODUCTION

Unani Medicine is a form of traditional medicine practiced in the middle-east & south-Asian countries. It refers to a tradition of Graeco-Arabic medicine, which is based on the teachings of Greek physician Hippocrates and Roman physician Galen, and developed into an elaborate medical system in middle age era by Arabian and Persian physicians, such as Rhazes (al-Razi), Avicenna (Ibn Sina), Al-Zahrawi, and Ibn Nafis.

Unani medicine is based on the concept of the four humours: Phlegm (Balgham), Blood (Dam), Yellow bile (Ṣafrā') and Black bile (Saudā'). The time of origin is thus dated at *circa* 1025 AD, when Avicenna wrote *The Canon of Medicine* in Persia. While he was primarily influenced by Greek and Islamic medicine, he was also influenced by the Indian medical teachings of Sushruta and Charaka.

In recent years, there has been great demand for plant derived products in developed countries. These products are increasingly being sought out as medicinal products, nutraceuticals and cosmetics. There are around 342 traditional manufacturers in Bangladesh. According to the DGDA, about 269 units are producing Unani medicines, 171 units are producing Ayurvedic medicines, 29 units are producing herbal medicines and 79 units are producing Homeopathic and Biochemic medicines with few exceptions. Due to lack of infrastructures, skilled manpower, reliable methods and stringent regulatory laws most of these manufacturers produce their products without following strict guidelines and quality control test parameters/ protocols.

In order to have a good coordination between the quality of raw materials, in process materials and the finished products, it has become essential to develop reliable, specific and sensitive quality control methods using a combination of classical and modern instrumental method of analysis. Standardization is an essential measurement for ensuring the quality control of such traditional medicines. "Standardization" expression is used to describe al measures, which are taken

during the manufacturing process and quality control leading to a reproducible quality.

It also encompasses the entire field of study from birth of a plant to its clinical application. It also means adjusting the plant derived preparations to a defined content of a constituent or a group of substances with known therapeutic activity respectively by adding excipients or by mixing together. "Quality Control" of such drug means confirmation of its identity and determination of its quality and purity and detection of its nature of adulteration.

The World Health Organization (WHO) has appreciated the importance of medicinal plants for public health care in developing nations and has evolved guidelines to support the member states in their efforts to formulate national policies on traditional medicine and to study their potential usefulness including evaluation, safety and efficacy.

Standardization of such traditional medicines is not an easy task as numerous factors influence the bio-efficacy and reproducible therapeutic effect. In order to obtain quality oriented herbs, care should be taken right from the proper identification of plants, season and area of collection and their extraction and purification process and rationalizing the combination in case of polyherbal drugs.

WHO also has developed a series of technical guidelines and documents relating to the safety and quality assurance of medicinal plants. These include, Guidelines on good agricultural and collection practices (GACP) for medicinal plants and Quality control methods for medicinal plant materials.

The quality of Unani medicines has a direct impact on their safety and efficacy. There are many control measures for Unani medicines, and first important step is to control the quality of medicinal plants and Unani materials. However, this is a very complicated and difficult task as it involves many different areas, such as the environment and agricultural practices.

In recent, China is a major producer and exporter of traditional medicines in the world and India is associate partner with China. They are trying to maintain the safety and efficacy of the plant materials as per WHO and other international health

organization. Recently, Department of AYUSH, Ministry of Health and Family Welfare, Government of India represents a Protocol for Testing of Ayurvedic, Siddha and Unani Medicines. They emphasis on various quality parameters for testing of single and combined formulations as per requirements of WHO and other International Health Organization.

Basically about 70% of active ingredients of Unani medicine are plant materials or plant products, nearly 10% of active ingredients are Bio-species and animal products and about 20% of active ingredients of Unani medicine are crude minerals & chemicals. The crude minerals and chemicals should be standardized in pre-formulation stages and finished products according the conventional pharmacopeial methods approved by the DGDA.

Therefore, rational drug management has become an increasingly important topic in order to make optimal use of the drug budget and to offer health services of the highest possible standard, safe and devoid of adverse drug reactions. Study of indigenous medicine including Unani in relation with drug safety and quality assurance is thus imperative. One of the difficulties has been that there are many complex issues relating to adverse event detection with traditional products. These include the problems of products with multiple ingredients, drugs of multiple systems of medicine, misclassification of names, poor standardization of products, lack of clinical trials, variation in manufacturing processes, contamination, adulteration and misidentification of herbs. In particular, rare adverse events and delayed effects may not be readily identified despite traditional use, countering the argument that many herbal remedies are safe because of previous traditional use. So, it is imperative to develop the Unani systems of medicine in Bangladesh setting up the standardization and quality parameters according to international health requirements.

Standardization of Unani Medicines:

Standardization of drugs means conformation of its identity and determination of its safety, quality and purity. Phytotherapeutic agents or Phytomedicines are standardized Unani preparations consisting of complex mixtures of one or more plants which are used in most countries for the treatment of various diseases. According to the WHO definition, Unani (herbal) drugs contain as active ingredients plant parts or plant materials in the crude or processed state plus certain excipients.

Basically the standardization of the Unani plant materials will be based on raw material and the finished products. The raw materials are includes –

1) Crude plants and plant parts
2) Mineral/ Crude mineral
3) Animal organ or part of animal

The Unani finished product includes –

1) Arq / Sharbat /Marwareed/ Qutoor/Saiyal (Distillates/Liquid/Syrup)
2) Majoon/Etrifal/ Jawarish/ Marham/Zimad/Khamira/Dawaul/Laque/Halua (Semi solid)
3) Sanoon / Sufoof/ Kushta (powder)
4) Tila/ Rowghan (Medicated Oil and Cream)
5) Habb / Qurs / (Tablet/Pills/Capsule)

Here, the most important factors are plant materials & plant products and try to find out the way to ensure the quality of finished products. Total quality of products depends on quality raw materials and quality in-process from raw materials cultivation to finished products distribution. In this case, major roles will be played quality plants materials, manufacturer, vendors or suppliers and or importers.

Definition for Unani Plant Materials and Products:

Crude Drugs:

In the Unani Systems of Medicine comprising of Unani preparations, drugs of plant, animal and mineral origin, are used in their natural or so called “Crude” forms singly or in their mixture or in combination, to make a compound preparation of formulation. Nearly 70 per cent of the Crude Drugs are obtained from the plant sources while about 10 and 20 per cent of the drugs are derived from animal and mineral sources respectively. The drugs of plant origin especially of herbaceous nature are frequently used as whole plant; otherwise their parts such as Root, Stem, Leaf, Flower, Seed, Fruit, modifications of Stem and Root, Bark of a Stem or Root, Wood, and their Exudates or Gums etc. constitute single drugs in the Traditional Systems of Medicine.

Unani medicines:

These include herbs, Unani raw materials, Unani preparations and finished products:

Herbs:

Herbs include crude plant material such as leaves, flowers, fruit, seeds, stems, wood, bark, roots, rhizomes or other plant parts, which may be entire, fragmented or powdered.

Unani raw materials:

Unani raw materials are either whole plants or parts of medicinal plants in the crude state. They include herbs, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs. In some countries, these materials may be processed by various local procedures, such as steaming, roasting, or stir baking with honey or other materials.

Unani preparations:

Unani preparations are the basis for finished Unani products and may include comminuted or powdered Unani materials, or extracts, tinctures and fatty oils, expressed juices and processed exudates of Unani materials. They are produced with the aid of extraction, distillation, expression, fractionation, purification, concentration and other physical or biological processes. They also include preparations made by steeping or heating herbal materials in water and/or in other materials.

Finished Unani products or Unani medicinal products:

Medicinal products of Unani preparations containing the active substances are made of one or more herbs. If more than one herb is used, the term mixed herbal products can also be used. They may contain excipients in addition to the active ingredients. Such traditional medicines also may contain natural inorganic and organic active ingredients of mineral and animal origin. Generally however, finished products or mixed products to which chemically defined active substances have been added, including synthetic compounds and/ or isolated constituents from different materials.

Medicinal plant:

A plant, either growing wild or cultivated, used for its medicinal purposes.

<u>Related Definitions:</u>

Odour:

The “odour” is examined by directly smelling 25 g of the powdered drug contained in a package or freshly powdered. If the odour is discernible the sample is rapidly transferred to an open container and re-examined after 15 minutes. If the odour persists to be discernible, it is described as having odour.

Taste:

The “Taste” of a drug is examined by taking a small quantity of 85 mesh powder by a tip of moist glass rod and applying it on tongue previously rinsed with water. This may not be done in case if poisonous drugs, indicated in monograph.

Contamination:

The undesired introduction of impurities of a chemical or microbiological nature or of foreign matter, into or onto a starting material, intermediate product or finished herbal product during production, sampling, packaging or repackaging, storage or transport.

Cross-contamination:

Contamination of a starting material, intermediate product or finished product with another starting material or unformulated materials or product during product manufacturing.

Foreign matter:

Material consisting of any or all of the following:

- Parts of the medicinal plant material or materials other than those named with the limits specified for the plant material concerned;
- Any organism, part or product of an organism, other than that named in the specification and description of the plant material concerned;
- Mineral admixtures such as soil, stones, sand, and dust; and glass, metal and plastics or any other extraneous materials. These may be loose or adhering to these medicinal plant materials.

Pesticide:

Pesticides are defined as any substance intended for preventing, destroying, attracting, repelling, or controlling any pest including unwanted species of plants or animals during production, storage, transport, distribution and processing. The term includes substances intended for use as a plant-growth regulator, defoliant, desiccant, fruit thinning agent, or sprouting inhibitor and substances applied to crops either before or after harvest to protect the commodity from deterioration during storage and transport. The term normally excludes fertilizers and plant nutrients.

Pesticide residues:

Pesticide residues are any specified substance in food, agricultural commodities or animal feed resulting from the use of a pesticide. The term includes any derivatives of a pesticide, such as conversion products, metabolites, reaction products and impurities considered to be of toxicological significance.

Mycotoxins /Aflatoxins:

The presence of mycotoxins in plant material can pose both acute and chronic risks to health. Mycotoxins are usually secondary metabolic products which are nonvolatile, have a relatively low molecular weight, and may be secreted onto or into the medicinal plant material. They are thought to play a dual role, fi rstly, in eliminating other microorganisms competing in the same environment and secondly, helping parasitic fungi to invade host tissues. Mycotoxins produced by species of fungi including *Aspergillus*, *Fusarium* and *Penicillium* are the most commonly reported.

Mycotoxins comprise four main groups, namely, aflatoxins, ochratoxins, fumonisins and tricothecenes, all of which have toxic effects. Aflatoxins have been extensively studied and are classified as Group 1 human carcinogens by the International Agency for Research on Cancer.

Raw material processing for Product Manufacturing:

All drug materials of plant, animal & mineral origin, being used in the manufacture of Unani medicine, procured locally or by importation, should invariable kept in the quarantine, as per existing procedure followed by pharmaceutical manufacturing companies in Bangladesh implemented by DGDA.

Quality control for starting drug materials and finished products of plant origin, any two or all of the following Quality Control Test should be carried out:

01. Identification Tests: (a) Macroscopic & Microscopic test
    (b) Qualitative Phytochemical test
    (c) TLC Method, HPTLC, HPLC, LCMS
    (d) Chemical, pesticidal, heavy metal, microbial tests etc
02. Quantitative Tests of one or more marker substance say Alkaloid, Glycoside, and Flavonoid etc

Over all the quality control parameters of the raw and finished products will include –

a) PHARMACOGNOSTICAL

- Taxonomical
- Morphological
- Anatomical
- Biological
- Biochemical
- Biotechnological

b) PHYSICO - CHEMICAL

- Ash Values
- pH
- Hardness
- Disintegration Time
- Elemental Composition

c) PHYTOCHEMICAL

- Extractive Values
- Chemical Profiling
- TLC Fingerprinting
- Markers
  - Bio-active
  - Biological
  - Chemical
- HPTLC / HPLC Based

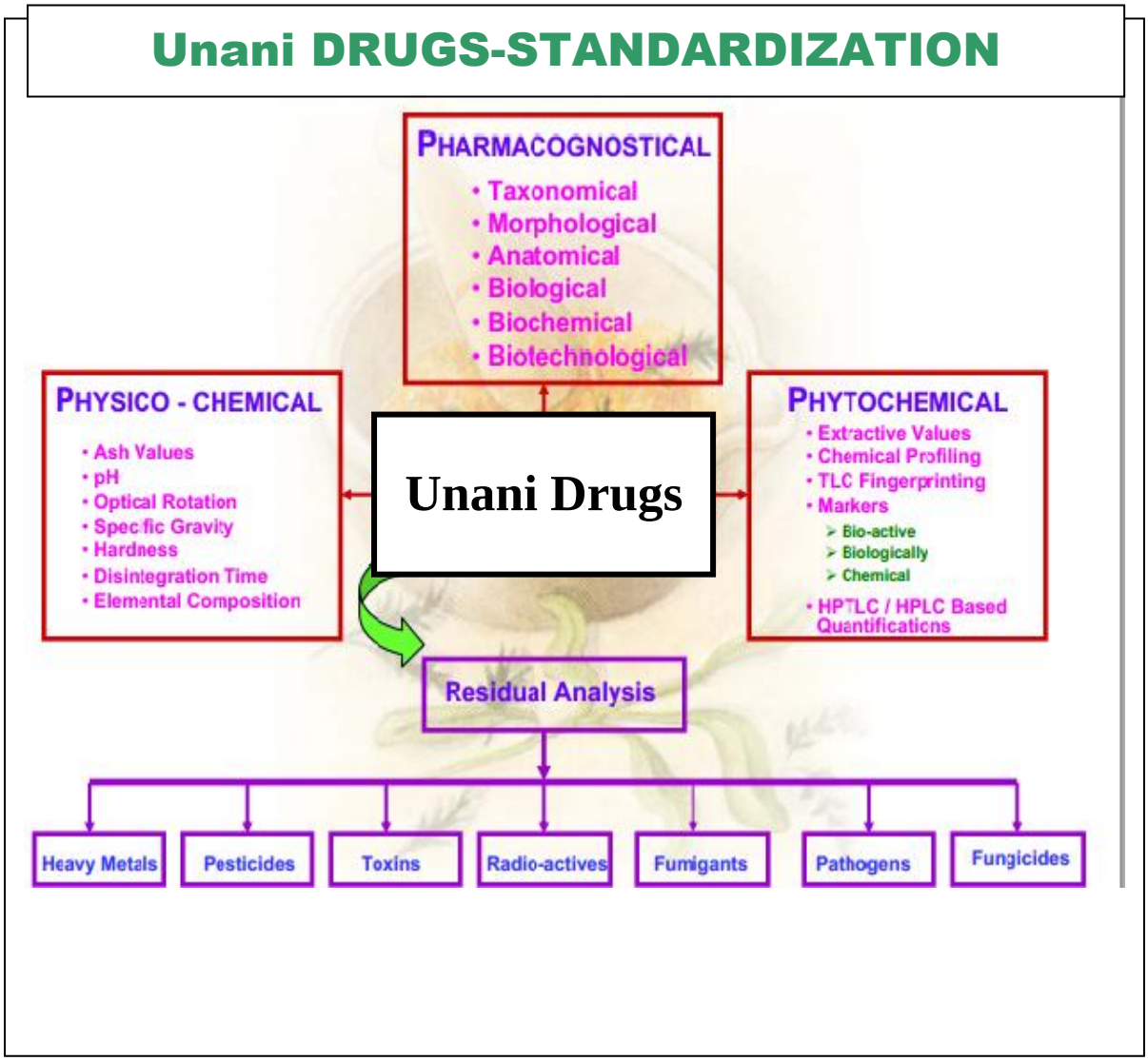
d) MICROBILOGICAL ANALYSIS

- Total viable count
- Presence of pathogenic organisms
  - *Escherichia coli*
  - *Salmonella* sp.
  - *Staphylococcus aureus*
  - *Pseudomonas* etc.

e) RESIDUAL ANALYSIS

- Heavy metals
- Pesticides
- Toxins
- Radio-actives
- Fumigants
- Fungicides

SUMMARY OF UNANI DRUGS STANDARDIZATION and QUALITY CONTROL PARAMETERS:



Types of Unani Medicine/Medicinal Products and Quality Control Parameters

1. Crude Unani materials

Quality control parameters –

- Authentication –

Each and every step needs to be authenticated

- area of the collection,
- parts of the plant collection,

- the regional situation,
- botanical identity,
- microscopic and
- histological analysis

If all or some parts of the parameter can authenticate, the material then authentication procedures should be considered accomplished.

As plant materials may contain heavy metals and /or pesticide residues they should be subjected to specific limit tests. However, the manufacturing company will get two years exemption from such tests. Then they have to implement these tests within the next four years.

2**.0 Mineral origin:**

Identification and relevant chemical test.

3.0 Animal organ or part of animal

Needs authentication and identification of animal, collection procedure, part of the animal or it organ, histological analysis.

Plant materials are processed as follows:

- Authentication of the plants material
- Keeping herbarium specimen for comparison and identification
- Assay of the liquid/dry extract is required considering at least one marker compound

Assay procedure includes any of the following,

- Titrimetric procedure (where ever possible)
- Spectrophotometric evaluation e.g. UV, IR etc
- Chromatographic evaluation. e.g. TLC, HPTLC, HPLC, GC, etc.
- Microbiological assay
- Total viable load (as described in BP or other official monographs or WHO guidelines enclosed in appendix)
- Presence of pathogenic organism (as described in BP or other official monographs
  or WHO guideline enclosed in appendix)
- Safety assay / Identification
- Assay/Identification for the presences of heavy metals. e.g Lead, Arsenic and Mercury

- Assay/Identification for the presences of pesticides

1. Tests and specifications of crude Unani plant materials are as follows

	Test	**Specification**
1	Appearance	Qualitative evaluation of the plant source, parts used, and its condition; e.g. whole plant, bark, leaves, dry or green etc. Comparing standard herbarium specification for proper identification
2	Characteristics	May be evaluated according to its organoleptic characteristic
3	Moisture content	Should be specific according to the type of plant or plant material/part
4	Foreign matters	Must comply with standard specification
5	Total ash	Must comply with standard specification
6	Identification	Macroscopic: Must comply with the standard specification. Microscopic: Must comply with the standard specification. UV Spectroscopy: comply with the absorption bands test after extraction Chromatographic: TLC, HPTLC, Densitometry evaluation, HPLC through evaluation of R_f values or retention time (R_t) of the reference and test sample; comparison with the fingerprint of test and reference
7	Water soluble materials	Must comply with standard specification
8	Heavy metals	Arsenic, Lead, Cadmium, Mercury, Copper etc
9	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)
10	Aflatoxins/ Mycotoxins	Should follow standard monograph;(BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not more than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb
11	Pesticide	Must comply with the standard recommended by standard

	residues	monograph (USP/WHO/EMA guideline)
12	Heavy metals	Arsenic: 5ppm Lead: 10ppm Cadmium: 0.3ppm Mercury: Nil Copper: Nil
13	Assay	Quantitative measure of the marker compound(s) in the test sample in comparison to reference compound(s)
Note: Tests 1, 2, 5, 6 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) and total aerobic microbial count and total combined yeast and mold counts are mandatory.		

2. Tests and specifications of Unani Plant Extract(s):

- Authentication of the plants material
- Keeping herbarium specimen for comparison and identification
- Assay of the liquid/dry extract is required considering at least one marker compound

Assay procedure includes any of the following,

- Titrimetric procedure (where ever possible)
- Spectrophotometric evaluation e.g. UV, IR etc
- Chromatographic evaluation. e.g. TLC, HPTLC, HPLC, GC, etc.
- Microbilogical assay
- Total viable load (as described in BP or other official monographs or WHO guideline enclosed in appendix)
- Presence of pathogenic organism (as described in BP or other official monographs or WHO guideline enclosed in appendix)
- Safety assay -
- Assay for the presences of Heavy metals, e.g Lead, Arsenic and Mercury
- Assay for the presences of pesticides

(WHO guideline enclosed in appendix)

	Test	Specification
1	Appearance	Qualitative evaluation of the plant source, parts used, and its condition; e.g. whole plant, bark, leaves, dry or green in reduced, powdered or cut etc.
2	Characteristics	May be evaluated according to its organoleptic characteristic
3	Moisture content	Should be specific according to the type of plant or plant material/part
4	Foreign matters	Must comply with standard specification
5	Total ash	Must comply with standard specification
6	Acid insoluble ash	Must comply with standard specification
7	Identification	Macroscopic: Must comply with the standard specification. Microscopic: Must comply with the standard specification. UV Spectroscopy: comply with the absorption bands test after extraction Chromatographic: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time ($R_{t)}$ of the reference and test sample; comparison with the fingerprint of test and reference
8	Water soluble materials	Must comply with standard specification
9	Heavy metals	Arsenic, Lead, Cadmium, Mercury, Copper etc
10	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)
11	Aflatoxins/ Mycotoxins	Should follow standard monograph (BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not More Than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb

12	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
13	Heavy metals	Arsenic: 5ppm Lead: 10ppm Cadmium: 0.3ppm Mercury: Nil Copper: Nil
14	Assay	Quantitative measure of the marker compound(s) in the test sample in comparison to reference compound(s)
Note: Tests 1, 2, 5, 6, 7 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) and total aerobic microbial count and total combined yeast and mold counts are mandatory.		

3. Tests and specifications of animal or its organ as raw material is Unani Medicine:

	Test	**Specification**
1	Appearance	Qualitative evaluation of the animal source, its organ, parts of organ etc to be used.
2	Characteristics	May be evaluated according to its characteristics
3	Histology	Must comply with standard specification
4	Identification	Must comply with standard specification
5	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)
6	Aflatoxins/ Mycotoxins	Should follow standard monograph (BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not More Than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb
7	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
8	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: Nil; Copper: Nil
9	Assay	Quantitative measure of the marker compound(s) in the test sample in comparison to reference compound(s)
Note: Tests 1 - 4 and total aerobic microbial count and total combined yeast and mold counts are mandatory.		

4. Finished Unani products or Unani medicinal products

The finished herbal product may be of following types –

a. Solid: Powder (Dusting, Effervescent/non-effervescent), tablet (Coated/non-coated), capsule (Hard/soft gelatin, HPMC, coated/non-coated/gastro-resistant)

b. Liquid: Syrup, Suspension, Emulsion, Elixir, Solution.

c. Semisolid: Cream, Ointment

d. Suppository: Considered for the future

e. Injectable: Considered for the future

Solid

Unani Powdered Raw Material:

	Test	Specification
1	Appearance	Qualitative evaluation of the powdered raw material considering color, odor, and particle size etc. (microscopic). Taxonomical test can be taken place where ever required.
2	Characteristics	May be evaluated according to its organoleptic characteristic
3	Moisture content	Should be specific according to the type of plant or plant material/part
4	Foreign matters	Must comply with standard specification
5	Total ash	Must comply with standard specification
6	Acid insoluble ash	Must comply with standard specification
7	Identification	Macroscopic: Must comply with the standard specification. Microscopic: Must comply with the standard specification. UV Spectroscopy: comply with the absorption bands test after extraction Chromatographic: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time ($R_{t)}$ of the reference and test sample; comparison with the fingerprint f test and reference
8	Water soluble materials	Must comply with standard specification
9	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: nil and Copper: nil
10	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of

		standard monograph)
11	Aflatoxins/ Mycotoxins	Should follow standard monograph (BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not more than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb
12	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
13	Assay	Quantitative measure of the marker compound(s) in the test sample in comparison to reference compound(s)
Note: Tests 1 to 3, 5 to 7 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) and total aerobic microbial count and total combined yeast and mold counts are mandatory.		

Unani Finished Products

a) Unani Tablet/Habb-e Preparation

	Test	Specification
1	Appearance	Size and shape: round, oval, oblong etc., color as defined
2	Average weight and uniformity	Average weight per tablet within considerable weight variation limit and uniformity must comply with the standard specification as per (Unani) monograph.
3	Hardness	Must comply with standard specification/monograph
4	Thickness	Must comply with standard specification/monograph
5	Friability	Must comply with standard specification/monograph
6	Moisture content	Must comply with standard specification/monograph
7	Disintegration	Test of disintegration as per the set specification
8	Dissolution	Must comply with standard specification/monograph
9	Identification/ Assay	*Titrimetric*: when identification and assay is possible through titration *UV Spectroscopy*: comply with the absorption bands and reference *Chromatographic*: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time ($R_{t)}$ of the reference and test sample; comparison with the fingerprint of test and reference
10	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: nil and Copper: nil

11	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)
12	Aflatoxins/Mycotoxins	Should follow standard monograph (BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not more than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb
13	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
Note: Tests 1 - 7, 9 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) and total aerobic microbial count and total combined yeast and mold counts are mandatory.		

b) Unani Capsule Preparation :

	Test	Specification
1	Appearance and material of shell	Size : 0, 00, 01, 02 etc color of the capsule shell as defined Shell: hard gelatin, soft gelatin, HPMC etc
2	Average weight and uniformity	Average weight of the capsule should comply with standard specification of the monograph. Uniformity of filled weight should also be within the range as per standard (Unani) monograph.
3	Disintegration	Test of disintegration as per the set specification
4	Dissolution	Must comply with standard specification/monograph
5	Identification/Assay	*Titrimetric*: when identification and assay is possible through titration *UV Spectroscopy*: comply with the absorption bands and reference *Chromatographic*: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time ($R_{t)}$ of the reference and test sample; comparison with the fingerprint region of test and reference
6	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: nil and Copper: nil

7	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)
8	Aflatoxins/ Mycotoxins	Should follow standard monograph;(BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not more than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb
9	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
Note: Tests 1 - 3, 5 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) and total aerobic microbial count and total combined yeast and mold counts are mandatory.		

c) Unani Granules /Powder Preparation

	Test	Specification
1	Appearance	Size : according to the mesh number as defined
2	Disintegration	Test of disintegration as per the set specification
3	Dissolution	Must comply with standard specification/monograph
4	Identification/ Assay	*Titrimetric*: when identification and assay is possible through titration *UV Spectroscopy*: comply with the absorption bands and reference *Chromatographic*: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time ($R_{t)}$ of the reference and test sample; comparison with the fingerprint region of test and reference
5	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: nil and Copper: nil
6	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)

7	Aflatoxins/ Mycotoxins	Should follow standard monograph (BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not more than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb
8	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
Note: Tests 1, 4 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) and total aerobic microbial count and total combined yeast and mold counts are mandatory.		

d) Unani Arq/Distillate Preparation

	Test	Specification
1	Appearance	Color: characteristic color should be defined Odor: characteristics odor should be defined
2	Distillation Temp	Must comply with standard distillation temp range according to specification /monograph
3	Identification/Assay	*Titrimetric*: when identification and assay is possible through titration *UV Spectroscopy*: comply with the absorption bands and reference *Chromatographic*: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time (R_t) of the reference and test sample; comparison with the fingerprint of test and reference
Note: Tests 1 to 3 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) are mandatory.		

e) Unani Semisolid (Paste) Preparation:

	Test	Specification
1	Appearance	Color : Should specific according to the formulation and comply with Odor : Characteristic odor according to the type of preparation and must comply with
2	pH	As per the set specification

3	Weight per mL	As per the set specification
4	Viscosity	As per the set specification
5	Identification/Assay	*Titrimetric*: when identification and assay is possible through titration *UV Spectroscopy*: comply with the absorption bands and reference *Chromatographic*: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time ($R_{t)}$ of the reference and test sample; comparison with the fingerprint of test and reference
6	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: nil and Copper: nil
7	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)
8	Aflatoxins/ Mycotoxins	Should follow standard monograph (BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not more than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb
9	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
10	Heavy metals	Arsenic: 5ppm Lead: 10ppm Cadmium: 0.3ppm Mercury: Nil Copper: Nil
Note: Tests 1, 2, 5 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) and total aerobic microbial count and total combined yeast and mold counts are mandatory.		

f) Unani Sharbat (Syrup or Suspension) Preparation:

	Test	Specification
1	Appearance	Color : Should specific according to the formulation and comply with Odor : Characteristic odor according to the type of preparation and must comply with standard specification
2	pH	As per the set specification (pH 4.0 – 6.5)
3	Weight per mL	As per the set specification
4	Viscosity	As per the set specification

5	Identification/ Assay	*Titrimetric*: when identification and assay is possible through titration *UV Spectroscopy*: comply with the absorption bands and reference *Chromatographic*: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time ($R_{t)}$ of the reference and test sample; comparison with the fingerprint of test and reference
6	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: nil and Copper: nil
7	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)
8	Aflatoxins/ Mycotoxins	Should follow standard monograph (BP/USP/WHO/EMA guideline); i.e. Aflatoxin B1: Not more than 2□g/kg, Sum of Aflatoxins B1, B2, G1, G2): not more than 4ppb
9	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
10	Heavy metals	Arsenic: 5ppm Lead: 10ppm Cadmium: 0.3ppm Mercury: Nil Copper: Nil
Note: Tests 1 to 3, 5 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) and total aerobic microbial count and total combined yeast and mold counts are mandatory. Determination of Propylene glycol, Glycerine and Sorbitol (as per official guidelines) in the preparation is mandatory to ensure safety.		

g) Unani Oil / Tila Preparation

	Test	Specification
1	Appearance	Color : Should specific according to the formulation and comply with Odor : Characteristic odor according to the type of preparation and must comply with
2	Weight per mL	As per the set specification

3	Viscosity	As per the set specification
4	Identification/Assay	*Titrimetric*: when identification and assay is possible through titration *UV Spectroscopy*: comply with the absorption bands and reference *Chromatographic*: TLC, HPTLC, Densitometric evaluation, HPLC through evaluation of R_f values or retention time (R_t) of the reference and test sample; comparison with the fingerprint of test and reference
5	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: nil and Copper: nil
6	Microbial contamination	Total aerobic microbial count: Less than 107CFU/g or CFU/ml Total combined yeast and mold count: Less than 105 CFU/g or CFU/ml *Escherichia coli:* Less than 103 CFU/g or CFU/ml *Salmonella:* Nil (1g or 1ml) *Staphylococcus aureus*: Nil (1g or 1ml) *Clostridia*: Nil (1g or 1ml) *Pseudomonas:* Nil (According to the type of organisms should follow specifications of standard monograph)
7	Pesticide residues	Must comply with the standard recommended by standard monograph (USP/WHO/EMA guideline)
Note: Tests 1 - 4 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) are mandatory.		

h) Unani Semisolid (Ointment) Preparation

	Test	Specification
1	Appearance	Should define
2	Types of ointment: O/W or W/O	Must comply with the specification
3	pH	As per the set specification (pH 4.0 – 6.5)**???**
4	Identification/ Assay	*Titrimetric*: when identification and assay is possible through titration *UV Spectroscopy*: comply with the absorption bands and reference *Chromatographic*: TLC, HPTLC, Densitometry evaluation, HPLC through evaluation of R_f values or retention time (R_t) of the reference and test sample; comparison with the fingerprint region of test and reference
5	Heavy metals	Arsenic: 5ppm; Lead: 10ppm; Cadmium: 0.3ppm; Mercury: nil and Copper: nil
Note: Tests 1 to 3 and 4 (TLC/ HPTLC spot test under UV lamps/ Phytochemical test) are mandatory.		

i) Tests Parameters and Specification of Unani Minerals are as follows:

Sl. No.	Test and specification
1.0	Description
	Color
	Odor
	Taste
2.0	pH
3.0	Loss on drying at 105 ^{o}C
4.0	Foreign matters
5.0	Solubility
6.0	Identification: Chemical test
7.0	Test for heavy/Toxic metals Mercury Lead Cadmium Arsenic
8.0	Assay: Chemical test
Note: Tests 1, 2, 3, 5 and 6 are mandatory.	

Conclusions

The pharmaceutical sector is a rapidly growing and priority sector in Bangladesh. The alternative/ traditional systems of medicines comprising of the Unani, Ayurvedic, Homeopathic and Herbal medicines are widely used for primary health care by 80% of the population in this subcontinent. Therefore, modernization of alternative/ traditional medicines should be emphasized and accomplished to meet the international standards.

Immediate and concerted efforts should be taken to attain the quality of these products to such a level of high standards and ensure sustainably of the quality control and quality assurance systems. To meet the increasing demands of alternative/ traditional medicines research and development of these medicines is very important.

For the development of the Unani/ alternative medicines collaborative research programs must be established between the industries and academia/ research institutions.

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