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Review Article

The Concept of *Abdāl-i-Adwiya* (Drug Substitution/ Therapeutic Interchange) in Unani Medicine: A Critical Appraisal

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A B S T R A C T

Background
The concept of drug substitution/ therapeutic interchange is an age old concept of Unani Medicine in which an appropriate substitute is allowed when the first desired drug is not available. The present review has been carried out to explore the concept of drug substitution pertaining to needs, principles, types and scientific validation studies.
Materials and Methods
The classical Unani literatures and various scientific journals indexed in PubMed, Medline, Science Direct, SCOPUS, Google scholars and Research gate pertaining to drug substitution, ethnobotanical survey, pharmacological actions etc. were reviewed.
Results
This review study has revealed that since ancient time, the Unani physicians have shown their interest on genuine drug substitution with strictly following set principles. After going through classical Unani literature, lists of rarely available, high cost, toxic and endangered Unani drugs have been made which reflects the importance and need of therapeutics interchange. A scientific study carried out on some main drugs and their substitutes have shown the presence of similar phytoconstituents in the first desired drugs and their respective substitutes.
Discussion
Today, many Unani drugs are not available due to geographical variation, over-exploitation, growing human population, high cost, forced import, deforestation, loss of habitat, extinction of rare plants etc. Presently, stress is given to introduce newer drugs, not to resolve other problems involved in the use of traditional drugs including therapeutic interchange. Scientific validation of the concept of drug substitution can resolve such problems and will provide quality Unani drugs with economic feasibility.
Conclusion
The effort should be made to investigate substitutes of rarely available and high cost Unani drugs through preclinical, clinical and phytochemical studies.

Keywords: *Abdāl-i-Adwiya,* Drug substitution, Principle of drug substitution, Therapeutic interchange, Unani Medicine

Introduction

The term Unani *Tibb* refers a medical system of Greek origin.[1] This system has later been established in Rome, Spain, Mediterranean region and Indian subcontinent. According to Unani principles, the human body is composed with seven basic components viz. element, temperament, humours, organs, pneuma, faculties and functions. This system is fundamentally based on Hippocratic doctrine of four humours viz. *dam* (sanguineous), *balgham* (phlegm), *safrā*' (bilious) and *sawdā*' (melancholic) which are present in the human body in an equilibrium.[2] These humours are associated with four qualities such as hot, cold, moist and dry which refers to the temperament of an individual humour. The temperament is expressed in pair of the above mentioned four qualities such as the temperament of sanguineous humour is hot and moist; the temperament of phlegm is cold and moist; the temperament of bilious humour is hot and dry; and the temperament of melancholic humour is cold and dry.[3] An imbalance in the quality or quantity of any one of the above mentioned humours and temperament is responsible for disease condition. Hence, the main aim of a Unani physician is to restore the balance primarily by aiding bodily faculties i. e. *Tabī'at Mudabbir-i-Badan* (medicatrix naturae).[2] Usually, four modes of treatment viz. *'Ilāj bi'l Tadbīr* (Regimenal therapy), *'Ilāj bi'l Ghidhā'* (Dieto-therapy), *'Ilāj bi'l Dawā'* (Pharmacotherapy) and *'Ilāj bi'l Yad* (Surgery) are applied for the treatment of any disease.[4] Pharmacotherapy is one of the important modes of treatment in which various drugs are used. The treatment is principally based on detoxification of the body through evacuation of morbid humours. It is believed that after evacuation of morbid humours, the organs and systems of the body are detoxified. Sometimes, the first desired drug is not available for treatment purposes which may be replaced with another drug having same action. The concept of drug substitution is an important concept of Unani Medicine which has yet not been discussed extensively.

Materials and Methods

The classical Unani and ethno-botanical literatures, scientific papers obtained from search engines like PubMed, Medline, Science Direct, Google Scholar, Research Gate and offline Journals were reviewed pertaining to the concept of *Abdāl-i-adwiya* (Drug Substitution/ therapeutic interchange); needs, principles and types of drug substitution; pharmacological actions and phytoconstituents of main and substitute drugs etc. The classical Unani literatures from the period of Razi (Rhazes) (865-925 AD) to Hakim Kabiruddin (1870 -1952 AD) were reviewed. Total 60 literatures including scientific papers were reviewed. Of them 36 literatures were selected for writing of this manuscript. The lists of rarely available, endangered, high cost, toxic and adulterated drugs have been prepared. The lists of first desired drugs and their appropriate substitutes according to various aspects have also been prepared. Scientific studies of certain main drugs and their substitutes carried out on the basis of active constituents present in such drugs. The keywords which employed for review of this article are *abdāl-i-adwiya*, drug substitution, Unani Medicine, need of therapeutic interchange and principle of drug substitution.

Results

Abdāl-i-Adwiya (drug substitution/ therapeutic interchange)

The idea of *Abdāl-i-Adwiya* (drug substitution) is a key feature of Unani pharmacotherapy[5]. This age old concept of Unani Medicine is defined as replacement of main drug with another drug which has same or closest pharmacological action to the first desired drug.[6] This concept is dealt on the basis of need, principles and therapeutic aspects of drug interchange for the management of various diseases. Despite being vital thought, much emphasis has not been given on the concept of the rapeutic interchange by Unani physicians.[5] Many Unani scholars even thought that sacred ancient physicians had not compiled a single treatise or even a chapter on drug substitution. It is mentioned in a book that *"it is the fact that our physicians did not think the subject of drug substitutes viable for their scientific learning. For no book short or exhaustive consisted any chapter on such a vital aspect of substitutes, their adverse effects and anti-dotes and no writer discussed the related problems either".*[7] But, this is not the fact, many Unani scholars have written books or chapters on this topic. The concept of drug substitution is also mentioned in classical Ayurvedic literature by the name of *"abhava pratinidhi dravya".*[8] The Ayurvedic physicians have recommended that use a functionally similar substitute in the absence of a desired first choice drug.[9] In Ayurveda, a rare or non-available drug is interchanged by a more readily available drug.[10]

Manuscripts on *Abdāl-i-Adwiya* (drug substitution) compiled by Unani scholars

The earliest record on the concept of *Abdāl-i-Adwiya* was found as '*Kitab fi Abdāl al-Adwiya al-Mufrada va al-Ashjar va al-Samugh va al-Teen*' which has been compiled by Feesagoras (Pythagorus) (570-485 BC). Some historical evidences have suggested that this oldest collection is available in the Ayasofia library which is presently located in Istanbul, Turkey. Many Arabic linguistic Unani scholars have also compiled several books on this topic viz. Tiyazooq (d. 708 AD) has compiled '*Kitab Abdāl al-Adwiya*'; Masar Joya al-Basri (d.730 AD) has written '*Abdāl-i-Adwiya*'; Yohanna bin Masoya al-Baghdadi al-Nasturi (d. 857 AD) has compiled '*Kitab al-Abdāl*'; Hunayn bin Ishaq al-Ibadi (d. 873) has written '*Abdāl al-Adwiya al-Mufradā'*; Ibn Jazar (d. 979 AD) has compiled '*Risala fi Abdāl al-Adwiya*' and

Abu Saeed Ibrahim Al-Maghrabi (d. 1162 AD) has written '*Al-Badliyat*'. Al-Maghrabi has also compiled a compendium on single drugs i.e., '*Kitab al-Fateh fi al-Tadavi min Jamee Sanuf al-Amraz va al-Shakavi*' which discussed 549 drugs with their substitutes. The history has suggested that some other books on drug substitution have also been compiled but their authors' names are not mentioned. These books are '*Kitab al-Abdāl ma Adam fi al-Hal*', '*Kitab al-Abdāl al-Aqaqeer al Ma'dni va al-Nabati va al-Haivania va Tafseer al-Ikyal va al-Awzan*', '*Risala fi Abdāl al-Adwiya alti Tanfaqd Wajud Hafi al-Waqt al-Hazir*' etc.[7,11] Other classical texts on drug substitution are '*Jam-i-ibn Masoya*' has been written by Ibn Masoya; '*Mayamir al-Jalinus', 'Maqale-jalinus fi al-Abda*' and '*Adwiya Mufradā al-Jalinus*' have been compiled by Galen; '*Tadbeer al-Asha'* and *'Jam-i-Armas*' were compiled by Armas; '*Jam-i-Hunayn*' written by Hunayn ibn Ishaq; '*Jamie-Bolas*' written by Hkm. Bolas; '*Maqale fi Abdāl-i-Adwiya al-Mustamila fi al-Tib va al-Ilaj*' which is commonly known as '*Kitab al-Abdāl*'. This classical text has been compiled by Zakaria Razi in 9th Century AD. This manuscript has been translated into Urdu and English by the Central Council for Research in Unani Medicine (CCRUM) and published in 1980, 1986 and 2000 AD, subsequently. This book contains substitutes of 122 drugs.[7] In addition to the above mentioned manuscripts, several other classical texts particularly based on single drugs have mentioned substitutes of single drugs. '*Al-Qanoon fi al-Tib*', the book of Ibn Sina (d. 1037 AD) has mentioned the substitutes of 63 single drugs.[12] Ibn Betar (1190–1248 AD) has mentioned the substitutes of 81 single drugs in '*Kitab al-Mufradat al-Adwiya va al-Aghdiā*'.[13-16] '*Zakheera Khawarizam Shahi*' the book of Ahmad Hasan Jurjani has mentioned the substitutes of 80 single drugs.[17] Ibn Hubal Baghadadi has depicted the substitutes of approximately 53 single drugs in '*Kitab al-Mukhtarat fi al-Tib*'.[18] Muhammad bin Ali al-Tabib has written a whole chapter on drug substitution in '*Taqveem al-Adwiya'*. The 35th chapter of '*Majmu-i-Ziai*' compiled by Zia Muhammad Masood has discussed the drug substitution. Some books on drug substitution have written in Persian language viz. '*Risal-i-Dar Abdāl-i-Adwiyat*' which has been compiled by Sabur ibn Sahl (d. 868 AD).[11] Other classical texts on drugs such as '*Kitab Minhaj-ud-Dukan*', '*Khazain al-Adwiya*' and '*Makhzan al-Mufridat*' have also mentioned substitutes of many single drugs.[20,21]

Need of Drug Substitution

The World Health Organization (WHO) has estimated that about 80% population of the world depends on herbal drugs for their health care issues. The Indian subcontinent is known to be one of the key biodiversity centres with approximately 45,000 plant species. Nearly 15,000 medicinal plants have been recorded in India, of them 7,000-7,500 plants are used medicinally.[22] The extensive role of plants in the healing of various ailments is epitomized by their exploitation in all the major systems irrespective of the fundamental philosophical premise.[23] The Unani pharmacopoeias have described approximately 90% botanical, 5% animal and 5% mineral origin drugs.[24] Presently, many plant, animal and mineral origin drugs are not available particularly where the Unani system of medicine is practising. Since ancient time, Unani physicians have given importance to the concept of drug substitution.[11] Razi has stated that *"usually, all drugs required for treatment are not available everywhere, so if the physician is unaware of substitutes which must be used in place of the main drug, the objectivity of the medical profession will be abolished".*[7] The followings are the needs of therapeutic interchange as described in Unani literature.

Non-availability of Drugs

The Unani system of medicine has been flourished in many countries where a diversity of medicinal plants and other drugs are available. The major problem in this regard is all drugs are not available everywhere. The '*Enquiry into Plants*' compiled by Theophrastus (372 - 286 BC) is considered as one of the earliest compilations especially on medicinal plants, described approximately 500 plant drugs, of them nearly 40 plants are still in use. The medicinal plants mentioned in the '*Enquiry into Plants*' are from different regions of the globe such as Egypt, Cyrenacia and Indian subcontinents.[25,26] Due to development of Unani Medicine into many regions, its pharmacopoeia changed time to time. The old Unani pharmacopoeias have mentioned drugs which are basically origin of Greece, Africa, Europe and Arab countries. The new Unani pharmacopoeias compiled by mainly Indian Hakims have mentioned drugs of basically Indian origin. In fact, the Unani pharmacopoeias have collection of drugs which belongs to various regions and their availability is not possible everywhere. In spite of geographical variation, other reasons such as over-exploitation, growing human population, high cost, forced import, deforestation, loss of habitat, extinction of rare plants are also blamed for non-availability of main drugs.[25,26] Ibn Sina has stated that "*the first desired drug may be substituted when it is not available*".[11] A report revealed that 22% to 42% of plant species of the world have now been endangered. The world is sinking one potential plant origin drug every two years.[27] Certain drugs are not available in all places particularly in India. For instance, In Unani Medicine, *Ammi majus* is considered as drug of choice for the treatment of vitiligo. But, this drug is indigenous to Egypt and was not available in India few years ago. Though, now it is cultivated in Jammu, India. Indian Unani physicians have mentioned the substitute of *Ammi majus* is *Psoralea corylifolia* which is indigenous to India.[11] The following Unani drugs are unavailable or rarely available especially in India (Table 1).

Table 1.Non-available/rarely available Unani drugs

Common name	Scientific name	Common name	Scientific name
Balsan	*Commiphora opoballasum* Linn.	Lajward	Lapis lazuli
Zarawand Taveel	*Aristolochia longa* Linn.	Lab Lab	*Dolichos lab-lab* Linn.
Berbahuti	*Aramia coccinia*	Mameesa	*Thalictrum foliolosum* Dc.
Paneer Maya	Seriparium	Badranjboya	*Mellisa parviflora* Benth.
Jund Bedastar	Castoreum	Abhal	*Juniperus communis* Linn.
Rasan	*Innula racemosa* Hook. f.	Izkhar Makki	*Cymbopogon jwarancusa* (Jones) Schult.
Sang-i-Saremahi	Silicate of lime	Ghariqoon	*Agaricus alba* Linn.
Dam-ul-Akhwain	*Dracaena cinnabari* Balf. f.	Heera Kasees	Sulphates of Iron
Zumurrad	Emerald	Turmus	*Lupinus albus* Linn.
Zehar Mohra	Serpentina	Aqeeq	Agate
Salajeet	Asphalt	Fad-i-Zehar Ma'dni	A mineral origin drug
Anzaroot	*Astragalus sarcocola* Dymock.	Shaker Teegal	Hemiptera
Saresham Mahi	Isinglass		

High Cost Drugs

The cost of some Unani drugs is very high and not possible to purchase for everybody. It is also a need to choose substitute of such drugs. After market survey in Indian market, it has been found that the cost of following drugs is too high (Table 2).

Toxic Drugs

Certain drugs are very toxic in nature, although they are used after detoxification. Till date, only few scientific reports are available regarding toxicity of such drugs. It is need of the hour to choose substitute of toxic drugs or their toxic report must be scientifically validated. A list of toxic Unani drugs is given in Table 3.

Table 2.High cost Unani drugs

Common name	Scientific name	Common name	Scientific name
Mushk	*Moschus moschiferous*	Ambar	Ambergris
Zafran	*Crocus sativus* Linn.	Marwareed	Pearl
Mastagi	*Pistachia lentiscus* Linn.	Almas	Diamond
Banafsha	*Viola odorata* Linn.	Gul-i-Babuna	*Matricaria chamomilla* Linn.
Abresham	*Bombyx mori*	Sandal Safaid	*Santalum album* Linn.
Marjan	*Corrallium rubrum*	Sandal Surkh	*Pterocarpus santalinus* Linn.
Yaqoot	*Red Carborandum*	Salajeet	Asphalt
		Saqmoonia	*Convolvulus scammonia* Linn.
Gaozaban	*Borago officinalis* Linn.	Ustukhuddus	*Lavandula stoechas* Linn.

Table 3.Toxic Drugs

Common name	Scientific name	Common name	Scientific name
Afiyun	*Papaver somniferum* Linn.	Habb-us-Salateen	*Croton tiglium* Linn.
Azaraqi	*Strychnos nuxvomica* Linn.	Madar	*Calotropis gigantean* (Linn.) R.Br.
Baladur	*Semecarpus anacardium* Linn.	Shokran	*Conium maculatum*
Dhatura	*Dhatura stramonium* Linn.	Farfiyun	*Euphorbia resinifera* Linn.
Bhang	*Cannabis sativa* Linn.	Turbud	*Operculina turpethum* A. Berger
Samulfaar	Arsenic	Gandana	*Allium ascalonicum* Linn. (L.) Silva manso

Seemab	Mercury	Ajwain Khurasani	*Hyoscyamus niger* Linn.
Neela Tutiya	Copper sulphate	Zangar	Verdegris
Unsul	*Urginea scilla*	Raskapoor	Calomole
Zarareeh	Cantharide	Ghandhak	Sulphar
Safaida Kashgari	Lead carbonate	Gonghchi	*Abrus precatorius*
Suranjan	*Colchicum luteum* Baker.	Arand	*Ricinnis communis* Linn.[28]

Endangered drugs

In India, there is a lacking in the application of scientific measures for systematic cultivation of medicinal plants and due to over exploitation of the nature, few medicinal plants used in Unani Medicine are now on the verge of becoming extinct. The Government of India has identified some medicinal plants as endangered (Table 4).[29]

Table 4.Endangered drugs

Common name	Scientific name	Common name	Scientific name
Luffah	*Atropa belladonna* Linn.	Kapur Kachri	*Hedychium spicatum* Ham ex Smith.
Tejpatra	*Cinnamomum tamala*	Kala Zeera	*Carum carvi* Linn.
Dandan-i-Feel	Elephant's teeth	Qarn al-Aiyal[11]	Stag Horn

Adulteration

The adulteration is a practice of substituting original crude drug partially or wholly with other similar looking substances but free from or inferior in chemical and therapeutic properties. The adulteration is mainly done for commercial purposes and financial benefits. The below mentioned drugs are being adulterated with following drugs (Table 5).[30]

Table 5.List of main drugs & their adulterants

S. No.	Main drugs	Adulterants
1.	Azaraqi *(Strychnos nuxvomica* Linn.*)*	*Strychnos nuxblanda, Strychnos potatorum*
2.	Ghafis *(Gentian olivieri* Griseb.*)*	Kutki *(Picrorhiza kurroa)*
3.	Luffah *(Atropa belladonna) leaves*	Ailanthus leaves
4.	Zafran *(Crocus* Linn. *sativus* Linn.*)*	Carthamus tinctorius
5.	Mur-Mukki *(Commiphora myrrha)*	Scented bdellium
6.	Qaranfal *(Eugenia coryophyllata)*	Mother clove, clove stalks
7.	Hilteet *(Ferula foetida)*	Limestone
8.	Afiyunasa *(Papaver* Linn. *somniferum* Linn.*)*	Lead shot
9.	Cardamom *(Elettaria cardamomum)*	Rodent faecal matter
10.	*Ipecacuanha*	Dextrin
11.	Powdered colocynth *(Citrullus colocynthis* (L.) Schard.)	Exhausted ginger powder

However, the World Health Organization has recommended the rejection of raw material, having more than 5% of any other plant part of the same plant (e.g. stem in case of leafy drug), even though they are derived from the authentic plant. Based on these standards, adulterated drug (whether intentional or unintentional) should be rejected. As per Good Manufacturing Practices Guidelines (schedules-T) for Ayurvedic, Siddha and Unani (ASU) drugs in the section 33EEA, ASU drugs are deemed to be spurious if it has been substituted by other drug.[31]

Principles of Drug Substitution/ Therapeutic Interchange

The ancient Unani scholars have agreed upon use of first desired drug for treatment purposes. In this regard, many Unani physicians have stated that "whenever possible, the first desired drug should be used" which reflects the importance of main drug for the treatment of diseases. In case of non-availability of good quality of main drug, it is advised that inferior quality of the same drug may be preferred. In some cases, when the first desired drug is not available, another species of same drug may also be preferred e .g. Podina Nahri (Panny Royal) is the substitute of Podina Kohi (Mentha).[7] The Unani physicians have also advised that another part of the main drug may also be prescribed in case of non-availability of that part of the drug which is desired. For instance, root is given in place of fruit and seed is substituted in place of leaves. Margosa *(Azadirachta indica)* leaves or bark is used as substitute of Margosa flowers. This shows the importance of use of different species of same plant drug and different parts

of the same drug. Though, interchange or substitution of different species and even different origin of the drug is permissible in Unani Medicine in case of non-availability of first desired drug, non-availability of similar species of the first desired drug, unavailability of inferior quality of same drug and other parts of the same drug etc. It is also important that a substitute drug may not have similar pharmacological properties in respect to all action; it may have similarity only in a particular pharmacological property. The Unani scholars have made certain principles for drug substitution.[5,7,32]

Yaksaniyat-i-Afā'l (Similarity in pharmacological action)

This is the most important criteria to select a substitute of any drug. A drug which is substituted to the first desired drug, it should have similar pharmacological action. The main and the substituted drugs which pharmacological properties are similar for particular purpose, they may be substituted for each other.[33] A list of substituted drug for a particular action is given in Table 6.

Yaksaniyat-i-Mizāj (Similarity in temperament)

The second principal for substitution is the first desired drug and its substitute should have similarity in their temperament. According to Unani theory, any drug acts by either its *mizāj* (temperament) or *madda* (matter/ physical properties) or by *surat-i-nauiyah* (specific form/ structure of the drug). Of them the mechanism of drug action by temperament is very important.[33] In Unani Medicine, the treatment is done on the basis of *ilaj bil zid* (heteropathy) in which the drug is given against the temperament of the disease.[34] By this principal the drug is altering the nature of the disease. A list of main drugs and their substitutes

Table 6.Main and substitute drugs having same pharmacological properties

S. No.	Main drugs	Substitutes	Indications/ Actions
1.	Bisfaij *(Polypodium vulgare)*	Aftimmon *(Cuscuta reflexa* Roxb.*)*	Malencholic diarrhoea
2.	Badranjboya *(Mellisa officinalis* Linn.*)*	Abresham *(Bombyx mori)*	Cardiotonic
3.	Parsiawshan *(Adiantum capillus-veneris* Linn.*)*	Banafsha *(Viola odorata)*	Asthma
4.	Badāward *(Fagonia arabica* Linn.*)*	Shahtra *(Fumeria officinalis* Linn.*)*	Chronic fever
5.	Jintiyana *(Gentiana lutea* Linn.*)*	Beekh Karafas *(Apium graveolens* Linn.*)*	Inflammatory diseases of liver and spleen
6.	Jadwar *(Delphinium denudatum* Wall.*)*	Zarambad *(Curcuma zedoaria* (Christm.) Roscoe*)*	Antidote
7.	Suranjan *(Colchicum leuteum* Baker.*)*	Barg-i-Hina *(Lowsonia inermis* Linn.*)* / Muqil *(Commiphora mukul* Linn.*)*	Gout[7]

Table 7.Main and substitute drugs having same temperament

S. No.	Main drugs	Substitutes	Temperaments	Indications/Actions
1.	Aftimoon (*Cuscuta reflexa* Roxb.)	Turbud (*Ipomea turpethum* (Linn.) Silva Manso)	Hot & Dry	Malencholia[7]
2.	Darunaj (*Doronicum hookeri* Hook. F.)	Zarambad (Curcuma zedoaria (Christm.) Roscoe) / Qaranfal (Eugenia caryophyllata)	Hot & Dry	Cardiotonic, Hemiplegia[7]
3.	Dibaq (*Viscum album* Linn.)	Muqil (*Commiphora mukul*)/ Abhal (*Juniperous communis* Linn.)	Hot & Dry	Resolvent[7]
4.	Hazar Jashan (*Bryonia alba* Linn.)	Darunaj (*Doronicum hookeri* Hook. f.)/ Bisbasa (*Myristica fragrans*)	Hot & Dry	Diuretic[7]
5.	Waj (*Acorus calamus* Linn.)	Kamoon (*Cuminum cyminum*)/ Rewand (*Rheum emodi* Wall. ex Meisn.)	Hot & Dry	Stomachic[7]
6.	Zarambad(*Curcuma zedoaria* (Christm.) Roscoe)	Sheetraj (*Plumbago zeylanica*)/ Darunaj (*Doronicum hookeri* Hook. f.)/ Tarkhashqooq Barri (*Cichorium intybus* Linn.)	Hot & Dry	Resolvent, Antidote[7]

7.	Zarawand Taweel (*Aristolochia longa* Linn.)	Zarambad (*Curcuma zedoaria* (Christm.) Roscoe)/ Anzaroot (*Astragalus sarcocola*)	Hot & Dry	Anti-helminthic[7]
8.	Zarawand Mudharaj Linn. (*Aristolochia rotunda* Linn.)	Zarambad (*Curcuma zedoaria*(Christm.) Roscoe)/ Bisbasa (*Myristica fragrans* Houtt.)/ Qust (*Saussurea lappa*)	Hot & Dry	Epilepsy[7]
9.	Hamama (*Amomum aromaticum*)	Waj (*Acorus calamus* Linn.)	Hot & Dry	Rheumatism[7]
10.	Habb al-Neel (*Ipomea hederacea* Jacq. Roxb.)	Shahm-i-Hanzal (*Citrullus colocynthis* Linn.)/ Mahu Dana (*Euphorbia nerifolia* Linn.)	Hot & Dry	Purgative[7]

on the basis of similarity in the temperament is mentioned in Table 7.

It is also advised that there should be similarity in degree of temperament of both drugs. For example, when the temperament of the first desired drug is Hot & Dry in 1st degree, the substitute should also have the same intensity of temperament. In some cases when such type of substitute is not available then substitute of more or low intensity of hot and dry tempered drug may also be preferred in order to reduce or increase the dose of the substitute.[7,32,33]

Yaksāniyat-i-Zāhiri Khususiyāt (Similarity in physical properties/ organoleptic characters)

This is the third principle of therapeutic interchange. The substitute and first desired drug should have similarity in physical or organoleptic characters. Many organoleptic characters mainly taste and smell is directly related to the pharmacological properties of drugs. For instance, bitter taste drugs usually possess blood purifier action. Spicy drugs produce carminative and antispasmodic effects and sour taste drugs produce astringent effect. Volatile containing drugs produce exhilarant, bronchodilator, decongestant and deobstruent effects. But, this principle cannot be applied on all drugs. Many drugs despite of having similarities in organoleptic properties, their pharmacological actions are very much different. Thus, ancient Unani physicians have suggested that this is a weaker principle for selection of substitutes and they have advised that this principle should not be applied frequently.[24] A list of Main and their substitute drugs which have similarities in organoleptic characters is given in the Table 8.

Yaksāniyat-i-Jins (Similarity in origin)

This is also a principle of drug substitution made by Unani scholars. In this case, the first desired and its substitute drugs should be from same origin. For example, when the main drug is of plant origin then its substitute should also be from the same origin. But, several times this principle couldn't be applied and the substitute is taken from other source of origin. For example, the substitute of *Jund Bedastar* (Castorium) (animal origin) is Mirch Siyah (Piper nigrum) and Waj (*Acorus calamus*) (*plant origin*). Similarly, calcinated and washed shell of an egg (animal origin) is considered as substitute of Tarasis (*Ceratopetalum gummiferum*) (plant origin).[7] A list of main drugs and their substitutes belongs from same origin is given in the Table 9.

Table 8.Main and Substitute Drugs Having Similarity in Physical Properties

S. No.	Original drugs	Substitutes	Indications/ Actions	Organoleptic characters
1.	Darchini (*Cinnamomum zeylanicum*)	Salikha *(Cinnamomum cassia* (L.) J. Persi)/ Kabab Chini *(Piper cubeba* Linn. f.)[7]	Digestive	Taste: Sweet Smell: Aromatic
2.	Salikha (*Cinnamomum cassia* (L.) J. Persi)	Darchini (*Cinnamomum zeylanicum*)[7]	Digestive	Taste: Sweet Smell: Aromatic
3.	Shahtraj *(Fumaria officinalis* Linn.*)*	Senna (*Cassia angustifolia*)[7]	Blood purifier	Taste: Bitter
4.	Na'Na (*Mentha piperita* Linn.)	Faudanj Nahri (*Mentha aquatica* Linn.)[7]	Digestive	Taste: Sweet
5.	Aftimmon (*Cuscuta reflexa* Roxb.)	Turbud (*Ipomea turpethem*)[7]	Malencholia	Taste: Bitter

6.	Filfil Safaid *(Piper alba)*	Zanjabeel (Zingiber *officinale* Roscoe.)[7]	Carminative	Taste: Pungent Smell: Aromatic
7.	Zanjabeel (Zingiber *officinale* Roscoe.)	Filfil abyaz (*Piper alba*) [7]	Carminative	Taste: Pungent Smell: Aromatic

Table 9.Main and Substitute Drugs Having Similarity in Origin

S. No.	Original drugs	Substitutes	Indications/ Actions	Origin
1.	Zarawand Taveel (*Aristolochia longa* Linn.)	Zarambad (*Curcuma zedoaria* (Christm.) Roscoe)	Antidote	Plant
2.	Zarawand Mudharaj (*Aristolochia rotunda* Linn.)	Zarambad (*Curcuma zedoaria* (Christm.) Roscoe)	Hepatoprotective	Plant[7]
3.	Zafran (*Crocus sativus* Linn.)	Qust (*Saussurea lappa*)	Diuretic	Plant[7]
4.	Waj (*Acorus calamus* Linn.)	Kamoon (*Cuminum Cyminum* Linn.)/ Rewand (*Rheum emodi*)	Diuretic, Digestive	Plant[7]
5.	Darunaj (*Doronicum hookeri* Hook. f.)	Zarambad (*Curcuma zedoaria*)/ Qaranfal (*Eugenia coryophyllata* Thunb.)	Cardiotonic	Plant[7]
6.	Jauz-ut-Teeb (*Myristica fragrans* Houtt.)	Sumbul (*Valeriana officinalis* Linn.)	Aphrodiasic	Plant[7]
7.	Sang-i-Jarahat (Soap stone)	Gil-i-Multani (Fuller's earth)	Astringent	Mineral[21]

Table 10.Main and Substitute Drugs are Similar in Action, Temperament & Origin

S. No.	Main drugs	Substitutes	Actions	Origin	Temperament
1.	Zarawand Taveel (*Aristolochia longa* Linn.)	Zarawand Mudharaj (*Aristolochia rotunda*)	Antidote	Plant	Hot & Dry[7]
2.	Darchini (*Cinnamomum zeylanicum* Linn.)	Salikha (*Cinnamomum cassia* (L.) J. Persi)	Digestive	Plant	Hot & Dry[7]
3.	Huzaz (*Berberis lyceum*)	Feelzahraj (*Berberis aristata* DC.)	Anti-inflammatory	Plant	Hot & Dry[7]
4.	Na'Na (*Mentha piperita* Linn.)	Faudanj Nahri (*Mentha aquatica* Linn.)	Digestive	Plant	Hot & Dry[7]
5.	Salikha (*Cinnamomum cassia* (L.) J. Persi)	Darchini (*Cinnamomum zeylanicum* Linn.)	Digestive	Plant	Hot & Dry[7]

Aqsām-i-Badal (Types of substitution)

Three types of drug substitutes are mentioned in Unani literature. This classification is based on various properties of drug such as pharmacological action, temperament, organoleptic characters and origin of the drug.

Badal-i-Aqrab (Closest substitute)

In this type, the substitute and main drug both should have similarities in their pharmacological action, origin and temperament.[5,32] The drugs mentioned in the table, their pharmacological action, origin and temperament are same (Table 10).

Badal-i-Qareeb (Closer to substitute)

In this type, substitute and first desired drug should have similarities in two of three characters such as pharmacological action, temperament and/ or origin.[5, 32] [Table 11(a)].

The drugs mentioned below in the table 11 (b) are similar in the pharmacological action and temperament but their origin is different [Table No. 11(b)].

Table 1 I (a).Badal-i-Qareeb

S. No.	Main drugs	Substitutes	Pharmacological actions	Origin
1.	Dar Sheesha'an (*Mrica nagi*)	Yanboot (*Ceratonia siliqua*)	Retentive	Plant[7, 21]
2.	Dohn al-Balsan (oil of *Balsamodendron opobalsamum*)	Dohn al-Kazi (oil of *Pandanus tectorius*)	Nervine tonic	Plant [7]
3.	Balchad (*Bambusa arundinaceae* Kunth.)	Kasni (*Cichorium intybus* Linn.)	Resolvent	Plant[7]

Table 1 I (b).Badal-i-Qareeb

S. No.	Original drugs	Substitutes	Actions	Temperament
1.	Farbiyoon (*Euphorbia resinfera* A. Berger)	Khar al-Hamam (Pigeon's faeces)	Rheumatism [7]	Hot & Dry
2.	Badranjboya (*Mellisa parviflora* Benth.)	Abresham (*Bombyx mori*)	Cardiotonic[7]	Hot & Dry
3.	Labani (*Liquidambar orientalis* Benth.)	Jundbedastar (Castorium)	Nervine tonic[7]	Hot & Dry
4.	Tarasis	Qishr Baiza Muharraq (Burnt egg shell)	Used in haemorrhage[7]	Cold & Dry

Badal-i-Bayīd (Remote substitution)

In this type, substitute and main drugs should be similar only in pharmacological action. This type is a less accepted of principle for therapeutic interchange.[5, 32]

When, the substitute and first desired drugs are similar in all three characters viz. pharmacological actions, temperament and origin. This is called '*badal-i-kulli*' (complete substitution), but when these drugs are similar only in few characters, it is known as *badal-i-juzvi* (partial substitution). *Badal-i-Kulli or Badal-i-Aqrab* is considered as most appropriate principle for therapeutic interchange. The most important principal for therapeutic interchange is similarity in pharmacological action. Remaining two principles potentiate to the substitution rather than themselves to become independent principles.[32]

Scientific Studies on Therapeutic Interchange

Parveen S et al. 2018 has carried out a research on Unani concept of drug, substitution and its validation on scientific parameters. In this study, physicochemical, phytochemical and analytical parameters of three plant origin drugs and their respective substitutes were studied. As per classical Unani literature the pharmacological action of *Terminalia Chebula* (TC), is astringent and for this property *Embelica Officinalis* (EO) is used as substitute of *Terminalia chebula.* Qualitative phytochemical study has shown that both the drugs have alkaloids, glycosides, flavonoids, phenols, terpens, tannins, quinines anthraquinones, coumarines, diterpenes, carbohydrates, proteins, fixed oil etc and the quantitative study has revealed that *Terminalia chebula,* contains gallic acid and ellagic acid 2.5% whereas *Embelica officinalis* possesses the same constituents as 0.5%. *Hyoscyamus niger* (HN) is used as substitute of *Datura stramonium* (DS) for sedative effect. Qualitative phytochemical study has shown that HN and DS possesses alkaloids, glycosides, flavonoids, phenols, terpens, tannins, quinines anthraquinones, coumarines, diterpenes, carbohydrates, proteins, fixed oil etc and the quantitative study has revealed that DS contains, atropine 0.030567% whereas HN contains the same constituents as 0.026470%. *Myristica frangrans* (MF) is used as substitute of *Syzygium aromaticum* (SA) for carminative purpose. Qualitative phytochemical study has shown that MF and SA possesses alkaloids, glycosides, flavonoids, phenols, terpens, aminoacids, tannins, quinines anthraquinones, coumarines, diterpenes, carbohydrates, proteins, fixed oil etc and the quantitative study has revealed that MF contains eugenol, 2931.097 µmol whereas SA contains the same constituents as 147.305 µmol. This study has validated the concept of drug substitution with evidences from phytochemistry.[5] Shastry JLN et al., 2013 has carried out a comparative study on the substitutes in Ayurveda. They used three plant origin drugs i. e. *Sausurea lappa used, Inula racemosa* and *Ricinus communis* in patients of bronchial asthma. This study has shown that *Sausurea lappa* and *Inula racemosa* possesses morphological, phytochemical and pharmacological similarities whereas *Ricinus communis* exhibited similarity in pharmacological activity.[34] Venkatasubramanian P only, 2010 has carried out a research work to validate the concept of drug substitution. In this study, they took two plant origin drugs viz. *Aconitum heterophylum* and its substitute *Cyperus rotundus.* They did phytochemical and pharmacological screening of

these drugs and found similarities in phytochemistry and pharmacological activity and drugs contain alkaloids, anthraquinone glycosides, cardiac glycosides, flavonoides, saponins, phytosterols and tannins. Both drugs showed anti-diarrhoeal properties in experimental animals.[35]

Discussion

Abdāl-i-Adwiya (drug substitution/ therapeutic interchange) is an age old concept of Unani Medicine which is defined as chosen of another drug due to some genuine reasons in place of the first desired drug having same pharmacological action.[32] This concept doesn't mean that adulteration with poor quality or substandard drug with main drug. This practice is done in Unani Medicine for the benefit of the patients since the Unani system of medicine has spread to many countries of the world, so the pharmacopoeias have described drugs from different habitat and several drugs which are mentioned in classical Unani, literatures, not available everywhere. Cost of many Unani drugs and over exploitation are also matter of concern especially for today's Unani practice. Ancient Unani physicians were very much aware about such type of problems. That's why, Razi has depicted that *'if a physician is not completely aware about the drug substitution, the objectivity and benefaction of medical profession would be ceased'.* He further stated that *'all the drugs are not available at all places, so a physician must know substitutes of each drug'.*[7] In Unani Medicine, a substitute drug is prescribed only for a particular pharmacological action. It is not necessary that a drug is substituted to the main drug in respect to all pharmacological actions. The classical Unani literatures have mentioned certain guidelines for substitution of drug. For instance, the substitute and main drugs should have similarities in their pharmacological action, temperament, physicochemicals properties/ organoleptic characters and origin which is classified as '*badal-i-aqrab*' (closest substitute) and this is considered as an appropriate therapeutic interchange.[22,32] In present study, the whole concept of drug substitution of Unani Medicine has been reviewed. After thorough literature review, lists of unavailable/ rarely available, high cost, toxic and endangered drugs have been prepared which reflects the importance and need of drug substitution. The principle of drug substitution as described in Unani literature has also been extensively reviewed. Certain scientific studies on the basis of morphological characters, pharmacologicals actions and phytochemical evaluation have shown same therapeutic efficacy of substitutes and main drugs which further potentiates the concept of therapeutic interchange.[5,35,36] In present scientific era, emphasis is always given to discover newer potential drugs and little attention has given to solve the problems involved in the use of traditional drugs including therapeutic interchange.[36] In Unani Medicine, the substitution of an appropriate drug seems to be intentionally selected for benefit of the recipients and can also overcome the depletion of rare drugs, thus lend a support in conservation and sustainability of medicinal plants and provide a quality herbal formulation with economic feasibility.[36]

Conclusion

In Unani Medicine, the concept of therapeutic interchange does not refer adulteration with low standard or poor quality drugs, only appropriate and genuine substitution is acceptable. The effort should be made to explore substitute of rare and high cost Unani drugs through systematic studies on today's modern parameters for validation of the concept of drug substitution which has yet not been extensively touched by the scientific fraternity. In this regard, first thorough ethnobotanical review pertaining to presence, of phytoconstituents in the first desired drugs and their substitutes may be carried out. Subsequently, The comparative pharmacological studies regarding efficacy of both drugs may also be carried out in animals and human being. In Unani Medicine, till date no such pharmacological study on modern parameters has been carried out in this regard.

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