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REGULATORY REQUIREMENT OF SAFETY AND EFFICACY FOR AYURVEDIC, SIDDHA AND UNANI DRUGS

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ABSTRACT

Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy together called AYUSH are the traditional medicine. Now Sowa Rigpa is also the part of traditional system of medicine. In Ayurveda, Siddha and Unani, the drugs are of textual reference as well as there are patent or proprietary drugs. The drug products should exhibit the expected therapeutic efficacy and must be safe for use. The type of safety and efficacy documents needed depends upon the nature of drug products. The requirements depend upon ingredients, indication, as well as the type of products i.e. products are classical or proprietary.

KEYWORDS: Drug & Cosmetic Acts, Drugs Rules, Schedule E(1).

INTRODUCTION

Traditional medicine means the skill, knowledge and practice of healthcare system based on theories, belief and experiences indigenous to a culture. In India the traditional medicine means Ayurveda system of medicine. Ayurveda is the ancient and sacred system of health care originated over 5000 years ago and was further enriched by the ancient Rishi's with Siddha and Yoga practices. Unani-Tibb that was known from period of Hippocrates came to India during 8th century AD. Similarly Homeopathy got blended with the Indian traditional medical practice due to similarity in its holistic medical philosophy and principles. Today in India, traditional medicine means Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy which are together call AYUSH. Now Sowa Rigpa is also the part of traditional system of medicine.

Regulatory definition of Ayurveda, Siddha and Unani Drugs

In India the drugs are principally regulated through the Drugs and Cosmetics Act 1940 and the Rules made their under. It was the Drugs and Cosmetics Rules 1945 for regulation of drugs, medical devices and cosmetics. Now there are- The Drugs Rules 1945, The Medical Device Rules 2017, The New Drugs and Clinical Trial Rules 2019 and The Cosmetics Rules 2020 for drugs, medical device, new drugs and cosmetics respectively.

In Drugs and Cosmetics Act 1940, there are 38 sections. The section 3 is about definition having defined a number of terms such as drug, cosmetics, manufacture, import, analysts etc. The clause (a) and sub-clause (i) of clause (h) of section 3 is about the definition of Ayurveda, Siddha and Unani drug. Clause (a) of Section 3 says- *Ayurvedic, Siddha or Unani drug includes all medicines intended for internal or external use for or in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals, and* manufactured exclusively in accordance with the formulae described in, the authoritative books of Ayurvedic, Siddha and Unani Tibb systems of medicine, specified in the First Schedule. Sub-clause (i) of clause (h) of Section 3 of Drugs and Cosmetics Act defines Patent or Proprietary medicines of Ayurveda, Siddha and Unani (ASU) system. In relation to ASU system, patent or proprietary medicine include *all formulations containing only such ingredients mentioned in the formulae described in the authoritative books of Ayurveda, Siddha or Unani Tibb systems of medicine specified in the First Schedule, but does not include a medicine which is administered by parenteral route and also a formulation included in the authoritative books as specified in clause (a).* The medicines defined in clause (a) of section 3 are of textual reference which are commonly called classical medicine of Ayurveda, Siddha and Unani system.

Schedules of Drugs and Cosmetics act

There are two schedules in drugs and Cosmetics Act called Schedule-I and II. Schedule-I is under section 3 (a) whereas the schedule-II comes under section 8 and 16. Schedule-I is the list of authoritative books for Ayurveda, Siddha and Unani Tibb System. There are 58, 31 and 14 books as authoritative books for Ayurveda, Siddha and Unani system of medicine (See table 1, 2 and

3). Schedule-II is about Standards to be complied with by imported drugs and by drugs manufactured for sale, stoked or exhibited for sale or distributed.

Table 1: Authoritative books of ayurveda system.

Sl. No.	Books
1	Arogya Kalpadruma
2	Arka Prakasha
3	Arya Bhishak
4	Ashtanga Haridaya
5	Ashtanga Samgraha
6	Ayurveda Kalpadruma
7	Ayurveda Prakasha
8	Ayurveda Samgraha
9	Bhaishajya Ratnavali
10	Brihat Bhaishajya Ratnakara
11	Bhava Prakasha
12	Brihat Nighantu Ratnakara
13	Charaka Samhita
14	Chakra Datta
15	Gada Nigraha
16	Kupi Pakva Rasayana
17	Nighantu Ratnakara
18	Rasa Chandanshu
19	Rasa Raja Sundara
20	Rasaratna Samuchaya
21	Rasatantra Sara Va Siddha Prayoga Sangraha—Part1
22	Rasatantra Sara Va Siddha Prayoga Sangraha—PartII (Edition 2006)
23	Rasa Tarangini
24	Rasa Yoga Sagara
25	Rasa Yoga Ratnakara
26	Rasa Yoga Samgraha
27	Rasendra Sara Samgraha
28	Rasa Pradipika
29	Sahasrayoga
30	Sarvaroga Chikitsa Ratnam
31	Sarvayoga Chikitsa Ratnam
32	Sharangadhara Samhita
33	Siddha Bhaishajya Manimala
34	Siddha Yoga Samgraha
35	Sushruta Samhita
36	Vaidya Chintamani
37	Vaidyaka Shabda Sindu
38	Vaidyaka Chikitsa Sara
39	Vidya Jiwan
40	Basava Rajeeyam
41	Yoga Ratnakara
42	Yoga Tarangini
43	Yoga Chintamani
44	Kashyapasamhita
45	Bhelasamhita
46	Vishwanathachikitsa
47	Vrindachikitsa
48	Ayurvedachintamani
49	Abhinavachintamani
50	Ayurveda-Ratnakara
51	Yogaratnasangraha
52	Rasamrita

53	Dravyagunanighantu
54	Rasamanjari
55	Bangasena
56	Ayurvedic Formulary of India and its Parts
57	Ayurveda Sara Samgraha
58	Ayurvedic Pharmacopoeia of India and its Parts.

Table 2: Authoritative books of siddha system.

Sl. No.	Books
1	Siddha Vaidya Thirattu
2	Therayar Maha Karisal
3	Brahma Muni Karukkadai (300)
4	Bhogar (700)
5	Pulippani (500)
6	Agasthiyar Paripuranam (400)
7	Therayar Yamagam
8	Agasthiyar Chenduram (300)
9	Agasthiyar (500)
10	Athmarakshamrutham
11	Agasthiyar Pin (80)
12	Agasthiyar Rathna Churukkam
13	Therayar Karisal (300)
14	Veeramamuni Nasa Kandam
15	Agasthiyar (600)
16	Agasthiyar Kanma Soothiram
17	18 Siddar‘s Chillarai Kovai
18	Yog Vatha Kaviyam
19	Therayar Tharu
20	Agasthiyar Vaidya Kaviyam (1500)
21	Bala Vagadam
22	Chimittu Rathna (Rathna) Churukkam
23	Nagamuni (200)
24	Agasthiyar Chillarai Kovai
25	Chikicha Rathna Deepam
26	Agasthiyar Nayana Vidhi
27	Yugi Karisal (151)
28	Agasthiyar Vallathi (600)
29	Therayar Thaila Varkam
30	Siddha Formulary of India (Part I)
31	Siddha Formulary of India and its Parts

Table 3: Authoritative books of unani system.

Sl. No.	Books
1	Karabadin Qadri
2	Karabadin Kabir
3	Karabadin Azam
4	Ilaj-ul-Amraz
5	Al Karabadin
6	Biaz Kabir Vol. II
7	Karabadin Jadid
8	Kitab-ul-Taklis
9	Sanat-ul-Taklis
10	Mifta-ul-Khazain
11	Madan-ul-Aksir
12	Makhzan-ul-murabhat
13	National Formulary of Unani Medicine
14	Unani Pharmacopoeia of India

Excipients

Pharmaceutical excipients are substances other than active substances contained in preparations, and they are used to increase the utility of the active substances and preparation, to make formulation process easier, to keep the product quality, to improve the usability, and so forth. The excipients to be used, however, must be pharmacologically inactive and harmless in the administered amount and must not interfere with the therapeutic efficacy of the preparations. Permitted excipients along with their standards i.e. additives, preservatives, antioxidants, flavouring agents, chelating agents etc. permitted in the Indian Pharmacopoeia (IP), Prevention of Food Adulteration Act, 1954 and Bureau of Indian Standard Act, 1986 are permitted for use in Ayurveda, Siddha and Unani drugs with conditions. The excipients shall be used in the permissible limits as prescribed and shall comply with the respective quality specifications, not exceeding any specified limits of usage therein, and except Hydrogenated vegetable oil. Only natural coloring agents as permitted under rule 26 of Prevention of Food Adulteration Rules, 1955 will be used for Ayurveda, Siddha and Unani drugs and additionally, colors permitted under Rule 127 of the Drugs and Cosmetics Rules, 1945 shall be used for Proprietary Ayurveda, Siddha and Unani drugs as defined in subclause (i) of clause (h) of section 3 of Drugs and Cosmetics Act, 1940, not exceeding any specified limits of usage therein. Preservatives and coloring agents shall be mentioned on the label for the information of the consumer as required under rule 161 of the Drugs and Cosmetics Rules, 1945.

Prevention of Food Adulteration Act and other related enactment and orders related to food regulations have been repealed. Now Food Safety and Standards Act, 2006 is an Act to consolidate the laws relating to food and to establish the Food Safety and Standards Authority of India for laying down science based standards for articles of food and to regulate their manufacture, storage, distribution, sale and import, to ensure availability of safe and wholesome food for human consumption and for matters connected therewith or incidental thereto.

Additives used in various processes and in formulating dosage forms shall be mentioned clearly with quantities used, in the application for licenses and the record for the same shall be maintained by the manufacturers. Manufacturers shall be responsible to ensure rationality, safety and quantity used of various excipients in the formulation. Some of the artificial sweeteners are also permitted for use in Ayurveda, Siddha and Unani proprietary medicine.

Safety and Efficacy requirement

Quality standard is a broad term and in reference to drug product, quality standard means controlling manufacturing material, man-power and process so that the product ready for sale or consumer use are of acceptable quality. It is widely agreed that drug products should be manufactured to a high standard quality and free from unexpected contamination as the drug products are frequently critical to human health and consequences of quality problems are toxicity or sub-potency. The quality standard and contamination free products can be assured through Good Manufacturing Practice (GMP). As per Rule 157 (1) of Drugs Rules 1945, the manufacture of Ayurvedic, Siddha or Unani drugs shall be carried out in such premises and under such hygienic conditions as are specified in Schedule T. The objectives of schedule T requires that- (1) raw material used in the manufacture of drugs are authentic, of prescribed quality and are free from contamination, (2) the manufacturing process is as has been prescribed to maintain the standard. (3) adequate quality control measures are adopted, (4) the manufactured drugs which is released for sale is of acceptable quality and (5) to achieve the objectives listed above, each licensee shall evolve methodology and procedures for following the prescribed process of manufacture of drugs which shall be documented as a manual and kept for reference and inspection.

The drug products should exhibit the expected therapeutic efficacy and must be safe for use. The type of safety and efficacy documents needed depends upon the nature of drug products. The requirements depend upon ingredients, indication, as well as the type of products i.e. products are classical or proprietary.

Classical medicine: Classical products are the formulation of ancient text having long history of uses. As these formulations are in use since long time and have appeared as safe when used as per the indication and direction. No safety study is required for the product permission of a classical Ayurveda, Siddha and Unani drug in all compliance with the text, however a published literature is required as experience of effectiveness. No safety study is required for the product permission of a classical Ayurveda, Siddha and Unani drug for manufacturing in a dosage form other than mentioned in text but for the efficacy a published literature is required. In case, a classical product is applied for product permission for new indication, no safety study is required. Here an evidence as proof of effectiveness for new indication is required. If may be required to show the published literature for effectiveness. New indication means an indication other than the indication mentioned for that product in the first schedule book.

For patent or proprietary medicines: No safety study is required for the product permission of a Patent or Proprietary Ayurveda drugs having ingredients as per text and indication is textual rationale. A pilot study as per relevant protocol ASU drug is required as evidence for proof of effectiveness. Additionally a published literatures of ingredients are also required. Safety study is required for the product permission of a Patent or Proprietary drugs having any of Schedule E (1) of Drugs

and Cosmetics Act. An evidence as proof for the effectiveness and published literature are also required. For licencing purposes, categories included in patent or proprietary medicine are- (i) Balya/ Poshak/ Muqawi/ Unavuporutkal/ Positive health Promoter, (ii) Saundarya Prasadak (Husane afza)/ Azhagh-sadhan and (iii) Aushadh Ghana (Medicinal plant extracts - dry/wet). Balya/ Poshak are the formulations having ingredients mentioned in books of First Schedule of the Drugs and Cosmetics Act and recommended for promotional and preventive health. Saundarya Prasadak are the formulation having ingredients mentioned in Books of First Schedule of the Drugs and Cosmetics Act and recommended for oral, skin, hair and body care. Aushadh Ghana are dry or wet aqueous or hydro-alcohol extract obtained from medicinal plants mentioned in books of First Schedule of the Act.

Conduct safety studies for Balya/Poshak as well as for Saundarya Prasadak, in case the formulation contains of any of the ingredients as specified in the Schedule E (1). The dry or wet extract of medicinal plant is prepared by using water (aqua), alcohol, hydro-alcohol or other organic solvent. No safety or efficacy study is required for aqueous extract of medicinal plant with ingredient and indication compliance with text. In case of aqueous extract for new indication, evidence for proof of effectiveness is required. In case of hydro-alcohol extract of medicinal plant with existing indication, published literature may be required as experience for effectiveness and no safety study is required. When the hydro-alcohol extract is for new indication, safety study and evidence for proof of effectiveness are required and additionally published literature may also be required. For medicinal plant extract of other than aqueous or hydro-alcoholic the requirements are safety study as acute, chronic and tetragenecity; evidence for proof of effectiveness and additionally the published literature may also be required.

Schedule E(1): List of Poisonous Substances

Schedule E(1) comes under Rule 161 (2) of Drugs Rules 1945. It is the list of poisonous substances under Ayurveda, Siddha and Unani system of medicine. There are separate list of poisonous substances for Ayurveda, Siddha and Unani medicine. For Ayurveda the number of vegetable origin, animal origin and mineral origin drugs listed in the schedule are 13, 1 and 7 respectively. For Siddha there are 17 drugs listed in the schedule and all are of vegetable origin. For Unani the number of vegetable origin, animal origin and mineral origin drugs listed in the schedule are 8, 2 and 9 respectively. Table 4, 5 and 6 enlist the Schedule E(1) drugs.

Table 4: Ayurvedic system.

Name of Drug	Scientific name or English equivalent	Source of Drug
Ahipena (Except seeds)	*Papaver somniferum* Linn. (Except seed)	Vegetable origin
Arka	*Calotropis procera* (Ait.) R.Br.	Vegetable origin
Bhallataka	*Semecarpus anacardium* Linn. f	Vegetable origin
Bhanga (Except seeds)	*Cannabis sativa* Linn. (Except seeds)	Vegetable origin
Danti	*Baliospermum montanum* Mull. Arg.	Vegetable origin
Dhattura	*Datura metal* Linn	Vegetable origin
Gunja (seed)	*Abrus precatorium* Linn. (seed)	Vegetable origin
Jaipala (seed)	*Croton tiglium* Linn.	Vegetable origin
Karaveera	*Nerium indicum* Mill	Vegetable origin
Langali	*Gloriosa superba* Linn	Vegetable origin
Parasika Yavani	*Hyoscyamus niger* Linn.	Vegetable origin
Vatsanabha	*Acontium chasmanthum* Stapf ex Holm.	Vegetable origin
Vishamushti	*Strychnox nuxvomica* Linn.	Vegetable origin
Shringivisha	*Acontium chasmanthum* Stapf ex Holm	Vegetable origin
Gauripashana	Arsenic	Mineral origin
Hartala	Arsenic trisulphide	Mineral origin
Manahashila	Arsenic disulphide	Mineral origin
Parada	Mercury	Mineral origin
Rasa Karpura	Hydrargyri subchloridum	Mineral origin
Tuttha	Copper sulphate.	Mineral origin
Hingula	Cinnabar	Mineral origin
Sarpa Visha	Snake poison.	Animal origin

Arka used for Bhawna before making Bhasma is exempted

Table 5: Siddha system.

Name of Drug	Scientific name or English equivalent	Source of Drug
Abini (Except seeds)	*Papaver somniferum* Linn.	Vegetable origin
Alari	*Nerium indicum* Mill	Vegetable origin
Attru thummatti	*Citrullus colocynthis* (L.) Schrad	Vegetable origin
Umathai	*Datura stramonium* Linn	Vegetable origin
Etti	*Strychnox nuxvomica* Linn.	Vegetable origin
Ganja (except seed)	*Cannabis sativa* Linn.	Vegetable origin
Kalappaki kizahangu	*Gloriosa superba* Linn	Vegetable origin
Kodikkalli (exempted for external use)	*Euphorbia tirucalli* Linn.	Vegetable origin
Chadurakkalli (exempted for external use)	*Europhorbia antiquorum* Linn.	Vegetable origin
Kattu Thumatti	*Cucumis trigonus* Roxb.	Vegetable origin
Kunri (except root)	*Abrus precatorious* Linn.	Vegetable origin
Cheramkottai	*Semecarpus anacardium* Linn. f	Vegetable origin
Thillai	*Exoecoria agallocha* Linn	Vegetable origin
Nabi	*Acontium ferox* Wall	Vegetable origin
Nervalam	*Croton tiglium* Linn	Vegetable origin
Pugaielai	*Nicotiana tobacum* Linn	Vegetable origin
Mancevikkalli (exempted for External use)	*Euphorbia* species	Vegetable origin

Table 6: Unani system.

Name of drug	Scientific name or English equivalent	Source of Drug
Afiyn (Except seeds)	*Papaver somniferum* Linn.	Vegetable origin
Bazur-ul-banj	*Hyoscyamus niger* Linn.	Vegetable origin
Bish	*Acontium chasmanthum* Stapf ex Holmes.	Vegetable origin
Bhang (Except seeds)	*Cannabis sativa* Linn.	Vegetable origin
Charas (resin) (Except seeds)	*Cannabis sativa* Linn.	Vegetable origin
Dhatura seed	*Datura metal* Linn	Vegetable origin
Kuchla	*Strychnox nux vomica* Linn.	Vegetable origin
Shokran	*Conium maculatum* Linn.	Vegetable origin
Darchikna	Hydrargryi perchloridum.	Mineral Origin
Hira	Diamond.	Mineral Origin
Ras Kapoor	Hydrargryi Subchloridum (calomel).	Mineral Origin
Shingruf	Hydrargryi bisulphuratum	Mineral Origin
Zangar	Cupri subacetas.	Mineral Origin
Sammul-Far	(Abyaz, Asfar, Aswad and Ahmar) (white, yellow, black and red, Arsenic).	Mineral Origin
Tootiya	Copper Sulphate	Mineral Origin
Para	Hydrargyrum	Mineral Origin
Hartal	Arsenic trisulphide (yellow).	Mineral Origin
Sanp (head)	Snake (head)	Animal Origin
Telni Makkhi	*Mylabaris cichorii* Linn *Mylabaris pustulata* Thumb. *Mylabaris macilenta*	Animal Origin

DISCUSSION

There is an increasing interest in traditional system of medicine. Ayurveda, Siddha and Unani system of medicine developed in Asia and the Indian subcontinent over the centuries. Ayurveda is the sacred system of health care, originated in India whereas Unani medicine originated in Greece and was introduced to India by the Arabs. Siddha system of medicine is practiced in Tamil speaking parts of India and abroad. Superficially, Ayurveda and Unani medicine appear to be alike as both emphasize the importance of temperament and the body fluids, the biological humours. In similar way Siddha system considers the human body consists of three humours, seven basic tissues and the waste products of the body. The equilibrium of humours is considered as a healthy state, and its disturbance or imbalance leads to disease or sickness.

The manufacture for sale or for distribution of ASU drugs are permitted under and in accordance with the

conditions of a licence issued for such purpose. A number of documents are required for manufacturing licence and product permission. Safety and efficacy are the primary requirement for medicinal products and the requirements depend upon ingredients, indication, as well as the type of products i.e. products are classical or proprietary. Schedule E(1) is the list of poisonous substances for ASU drugs. Safety study is required in case of formulation contains Schedule E(1) particularly for patent or proprietary drugs. Proof of effectiveness is required either as published literature, or pilot study as needed. In certain cases published literature of ingredients are also required.

CONCLUSION

Safety and efficacy are the requirement for drug products including Ayurveda, Siddha and Unani medicine. Classical medicines are the formulations of ancient text having long history of uses. No safety study is required for product permission of classical Ayurveda, Siddha and Unani drugs. Safety study is required in case of formulation contains Schedule E(1) particularly for patent or proprietary drugs. The proof of effectiveness depends upon the type of product.

REFERENCES

1. Anonymous. Chapter I Introductory. In: Commercial's Manual on Drug & Cosmetics, Garg RA. Delhi, Commercial Law Publishers (India) Pvt. Ltd., 2018; 10: 01-06.
2. Anonymous. Schedule I, The Drug & Cosmetics Act 1940. In: Commercial's Manual on Drug & Cosmetics, Garg RA. Delhi, Commercial Law Publishers (India) Pvt. Ltd, 2018; 10: 54-57.
3. Anonymous. Schedule II, The Drug & Cosmetics Act 1940. In: Commercial's Manual on Drug & Cosmetics, Garg RA. Delhi, Commercial Law Publishers (India) Pvt. Ltd, 2018; 10: 57-59.
4. Anonymous. Part XIX Standards of Ayurvedic, Siddha and Unani Drugs, The Drug & Cosmetics Rues 1945. In: Commercial's Manual on Drug & Cosmetics, Garg RA. Delhi, Commercial Law Publishers (India) Pvt. Ltd, 2018; 10: 208-211.
5. Anonymous. The Food Safety and Standard Act 2006. In: Commercial's The Food and Safety Standard Act 2006, Gupta Virag. Delhi, Commercial Law Publishers (India) Pvt. Ltd, 2021; 14.
6. Anonymous. Part XVI Manufacture For Sale of Ayurvedic (Including Siddha) or Unani Medicine, The Drug & Cosmetics Rues 1945. In : Commercial's Manual on Drug & Cosmetics, Garg RA. Delhi, Commercial Law Publishers (India) Pvt. Ltd, 2018; 10: 194-203.
7. G.R.S 227(E). The New Drugs and Clinical Trials Rules 2019. In Notification Ministry of Health and Family Welfare, The Gazette of India, 2019; 19.
8. G.R.S 763(E). The Cosmetics Rules 2020. In Notification Ministry of Health and Family Welfare, The Gazette of India, 2020; 15.
9. G.R.S 78(E). The Medical Device Rules. In Notification Ministry of Health and Family Welfare,The Gazette of India, 2017; 31.
10. https://www.who.int/health-topics/traditional-complementary-and-integrative-medicine#tab=tab_1 (Cited on 14th August, 2023; 16: 58.