CHAPTER 1

Introduction

This chapter sets the background for the thesis work, leading up to aims and objectives. The history and evolution of the APD concept is also briefly mentioned.
1. **Abhāva Pratinidhi Dravya**

1.1 **Dependency on Plants for Medicine**

WHO estimates that, about 80 % of the global population depends on traditional systems of medicine for health care (WHO, 1998). Medicinal plants constitute an important source of traditional medicines like Ayurveda, Chinese, Tibetan, Homeopathy and Unani. Modern medicine is also dependent on herbs for several compounds like artemisinin, which is obtained from the antipyretic plant *Artemisia annua* of traditional Chinese medicine (Willcox and Bodeker, 2004). Popularity of herbal medicine has increased the demand for medicinal plants/herbal drugs. Medicinal plants are an integrated part of the culture in many societies.

A survey of 2004-05 estimated the national demand for medicinal plants as more than 3,19,500 MT (valued at Rs 1,069 Crores) which is increasing constantly. More than 2,400 species of medicinal plants are used by the codified systems of medicine in India. About 85% of the traded/ exported medicinal plants are sourced from the wild. There are 8,343 registered herbal drug manufacturing units in India, registered with the state drug controllers (Anonymous, 2002; Ved and Goraya, 2008). Table 1.1 gives the species of medicinal plants used in Indian systems of medicine along with the manufacturing units depending on crude drugs for medicine production.

1.2 **Medicinal plants are under threat**

The populations of several medicinal plant species in high trade are under threat of decline. Species such as *Coscinum fenestratum*, *Aconitum heterophyllum*, *Saraca asoca* etc. have limited and niche distribution in their natural habitats (Sarin, 2008).
Table 1.1: Medicinal plant species used in Indian systems of medicine (Adapted from Ved and Goraya, 2008)

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>System</th>
<th>Medicinal plant species used (No.)</th>
<th>Registered manufacturing units (No)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ayurveda</td>
<td>1,587</td>
<td>7,149</td>
</tr>
<tr>
<td>2</td>
<td>Siddha</td>
<td>1,128</td>
<td>309</td>
</tr>
<tr>
<td>3</td>
<td>Unani</td>
<td>503</td>
<td>270</td>
</tr>
<tr>
<td>4</td>
<td>Tibetan Medicine (Sowa-Rigpa)</td>
<td>253</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>Homeopathy</td>
<td>468</td>
<td>615</td>
</tr>
<tr>
<td>6</td>
<td>Western Medicine</td>
<td>192</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>2,400</strong></td>
<td><strong>8,343</strong></td>
</tr>
</tbody>
</table>

Ministry of Environment and Forests (MoEF), Government of India has recognized the endangered status of such species as early as 1992 and imposed a ban on their exports by introducing them in the negative list of exports (Zoo rules, 1992). Further exploitation may push them towards the threat of extinction. Conservation strategies are required for their protection. Cultivation of some endangered medicinal plants have been undertaken at various levels including by Government agencies, NGO’s, Ayurvedic drug industries and individual as a resource augmentation effort, with moderate success. An EXIM bank publication states that, only about 10% of the traded medicinal plant species are cultivated. It also reports that, around 66% of the plant species obtained from the wild are harvested destructively, causing severe threat to the population of medicinal plants (Anonymous, 2003). Cultivation efforts of several species are not successful for several reasons including the requirement of specific agro-climatic conditions (Nautiyal, 2004). A situation of high demand and lack of sustainable cultivation is putting an enormous pressure on the availability of genuine bio-resources (Ved and Goraya, 2008). Substitution and adulteration
by other raw drugs have crept into the markets. The legitimacy of such substitution has not been scientifically researched (Venkatasubramanian et al., 2010).

### 1.3 A Solution from Ayurveda to address non availability of medicinal plants

The problem of non-availability of certain medicinal plants probably existed in earlier times as well; centuries before globalization of Ayurveda and industrial mass-production of Ayurvedic medicine. Bhāva Miśra, a 15th Century Ayurvedic scholar in his work, Bhāvaprakāśa Samhitā introduces a concept called *Abhāva Pratinidhi Dravya* (APD) as a solution to address non-availability of medicinal plants (Chunekar, 2004). It has been suggested in Bhāvaprakāśa Samhitā and other texts that in the absence of an intended unavailable drug (*Abhāva Dravya- AD*), an alternative drug (*Abhāva Pratinidhi Dravya- APD*) can be used. Eg- In the absence of *Chitraka* (*Plumbago zeylanica* L.), *Danthī* (*Baliospermum montanum*) or *Apāmārga kṣāra* (alkaline preparation of *Achyranthes aspera*) have been mentioned in Yogaratnākara (Sastry, 2002) as substitute drugs. In practice as well it is observed that substitutes are used; many of which do not get mention in classical Ayurvedic texts, but are found in trade or used by physicians. Eg- Use of *Ipomoea mauritiana* tubers in the place of *Pueraria tuberosa* tubers as *Vidārī* (Venkatasubamanian et al., 2009).

While the concept and suggestions on the use of substitutes finds a general mention as early as Charaka Samhitā (15th Century BCE; Sastry, 1997a), introduction of APD is found in books written after the 14th Century, during the late medieval period. Ayurvedic texts including Bhāvaprakāśa Samhitā (Misra, 2002), Yogaratnākara (Sastry, 2002), Bhaiṣajya Ratnāvalī (Mishra, 2007) mention substitutes.
1.4  *Abhāva Pratinidhi Dravya*—Etymology and details

In the context of Ayurveda, *Abhāva Dravya* is a drug, which is rare or not easily available. In Sanskrit dictionaries it is explained as

"भतो भावोभावम्। नाभाव उपलब्धे:' (gato bhāvo abhāvam, nābhāva upalabdhehe)"

(Tarkavachaspati, 1990). ‘Unavailability’ or ‘absence’ of a material is called as *Abhāva*.


The word ‘*pratinidhi*’ means, ‘a representative’, ‘substitute’ or ‘deputy’ (Apte, 2005).

‘*Dravya*’ is a material, medicine or food capable of bringing some physiological changes in the living system. Therefore, ‘*Abhāva Pratinidhi Dravya*’ (APD) is a substitute drug, which can be used instead of the original drug for medicinal purposes. In this context AD, need not be a complete or absolute absence of certain herb or drug, it may be just difficult to obtain.

Availability may be an issue depending on

- **Season**: Some drugs like *Parpaṭa* (*Mollugo cerviana* or *Oldenlandia corymbosa*) are available only in rainy season, not during summer (Rameshkumar and Sivasudha, 2012)

- **Endemicity**: *Ativiṣā* (*Aconitum heterophyllum*) is endemic to Northern Himalayas and not easily available elsewhere (Sarin, 2008)

- **Quantity**: Drug industry may need large quantities of crude drugs, which may not be available in the required quantity. Eg- Ayurvedic drug industry has a huge demand of 2000 MT for the bark of *Aśoka* (*Saraca asoka*). However this has restricted
geographical distribution and limited populations which is inadequate to supply the trade volumes (Ved and Goraya, 2008)

- **Quality:** Several times, the quality of obtained drug may not be good. Mature tubers of *Pueraria tuberosa* are the Vidārī. However, to compensate the volumes needed, many times immature tubers are also added, which compromises the quality (Venkatasubramanian et al., 2009)

- **Cost:** Certain crude drugs are very expensive. *Keśara* (saffron - *Crocus sativus*) would cost not less than Rs 150/- per gram in retail market (Kashmir, 2015). This is often substituted with the stamens of *Carthamus tinctorius* or adulterated with coloured cotton threads (Hagh-Nazari and Keifi, 2013).

The above reasons could push the industry and sector to substitute with other available herbs.

1.5 **History of APD concept**

A cursory glance over the ancient Ayurvedic literature shows that, the APD concept of Ayurveda evolved gradually due to the need for identifying substitutes for unavailable drugs. Figure 1.1 depicts the timeline of evolution of the APD concept in Ayurveda.

1.5.1 **Early Ayurvedic literature (up to 7th Century BCE)**

In *Sūtra Sthāna*, 4th chapter, Charaka Samhitā mentions that a wise physician need not stick to the list of herbs mentioned in the books for treatment purposes; instead he can opt for other herbs that have similar properties and action (*guna-karma*). He uses the word ‘*anuktārthā*’, to indicate the drugs which are not mentioned in the text. However, such a liberty of selecting drugs that are not listed in the texts is given only to wise physicians who can use their analytical capacity to identify new drugs (Sastry, 1997a). Roots of *Eraṇḍa* are indicated by Suśruta Samhitā and its commentator Dalhaṇa instead *Gokṣura* in the context
of laghupanchamūla (Suśruta Samhitā, Sūtra Sthāna, 38/66) (Acharya, 1992). This has been supported by later written texts like Siddhasara Samhita (Ghildhiyal et al., 2013). Aṣṭānga Sangraha also permit the use of substitute herbs by the Vaidya (physician) (Murthy, 2002a).

“स्वल्कश्यानुमानयुक्ति कुशलाना अनुकार्थ्य ज्ञानयेति।”

(Swalakṣanyānumānayukti kuśalānām anukārthā jñānayeti) (Charaka Samhitā, Sūtra Sthāna, 4/20-21) (Sastry, 1997a).

Historical text, ‘Arthaśāstra’ of Kauṭilya Chaṇkya documents that, substitution/adulteration practices of plant drugs because of their high demand (Krayavikraya) (Shamasasry, 2014).

1.5.2 Ayurvedic literature of medieval period (8th century -15th century CE)

From the Ayurvedic literature of medieval period, it appears that the problem of non-availability of herbs was quite common and thus the concept of drug substitution was well formed. Tenth century Ayurvedic writer, Chakrapāṇi, the commentator of Charaka Samhitā comments on the statement of Charaka as (section 1.5.1),

(भूयो दर्शनात्त अवदार्थ तद्दृष्टि से अन्त्यप्राप्ति द्राक्षा पयो विदार्थौ तज्जातिघतन जीवनानि इत्युपमीयते।)

(Bhuyo darśanāt avadārya tadgeṣṭā prīti drākṣā payo vidārayādau tajjātiyathvena jīvanāni ityamumīyate) (Chakrapāṇi, Charaka Samhitā, Sūtra Sthāna, 4/20-21) (Sastry, 1997a)

“A (wise) physician can select other drugs (those which did not get described in the text) based on their properties. Drākṣā, milk and Vidārī could also be prescribed (in place of Jīvantī) because of jīvanīya (nourishing), snidhā (unctuous) and śīta (cool) properties” (Sastry, 1997a). Aṣṭānga Sangraha also accepts this opinion (A.S.Su.15) (Murthy, 2002a). Use of Piṇḍatagara is indicated the place of Tagara (Sastry, 1997a).
Commentators of Brhatrayis also allow use of some alternative herbs in the context of specific disease conditions. Use of anjana (eye solves) likes rasānjana and souvīrānjana instead of srotoanjana is allowed by Dalhaṇa. Substitution of Haiṭakī in the place of Dantī as a virechaka (purgative). Use of Eraṇḍa instead of Gokṣura and Padmaka in the place of Guḍūchi has also been recommended in (Acharya, 991; Sastry, 1997a).

Fifteenth century Ayurvedic scholar Bhāva Miśra says,
राजानामप्यपर्यत्पर्यत्त ततो अयतिदुर्लभा तस्मादस्य प्रतिनिधिः गृहीतात् तत् गृणं भिषक्।
(Rājnāmapyaṣṭavargastu tato apyatidurlabhā.

Tasmādasya pratinidhim grāhīyat tadgunam bhīṣak) (Bhavaprākṣa, Haritakyādi Varga, 143) (Chunekar, 2004).

“Certain drugs like the ‘Aṣṭavarga’ group of medicinal herbs are extremely rare and not available to treat even kings. Therefore the Vaidya can use substitute drugs having similar
guṇas (properties). In the next verse he enumerates the substitutes for Aṣṭavarga drugs. The substitutes suggested by Bhāva Miśra for Aṣṭavarga drugs are commonly available. E.g., for Medā-Mahāmedā (Polygonatum cirrhifolium (Wall.) Royle) he has suggested Śatāvari (Asparagus racemosus) and for Kākoli (Lilium polyphyllum D. Don.) and Kṣirakākoli (Fritillaria roylei Hook.f.), Vidāri (Pueraria tuberosa) has been suggested as substitutes.

1.5.3 Ayurvedic literature of modern period (15th century CE onwards)

The 17-18th century CE Ayurvedic works like Bhaisajya Ratnāvalī (Mishra, 2007) and Yogaratnākara (Sastry, 2004) mention APDs for many Abhāva- Pratinidhi Dravyas. However, they also do not mention the logic behind substitution or any details about the parts to be used.

1.6 Unexplored Ayurvedic concept

The Ayurvedic concept of APD has thus far not been systematically and scientifically studied. Even if studied the research is not published. The list of plant drugs and their substitutes as per Ayurveda is not available in one place. The scientific basis of drug substitution and the Ayurvedic logic behind identifying substitute drugs are also not described or published. On observing the contemporary practice, it is clear that, the APD concept is not well utilized even by the current day Ayurvedic practitioners, except some. There is also a lack of common awareness about the possibility of using APDs in the place of rare and endangered APDs across Ayurvedic scholars and scientists involved in herbal drug manufacturing. Some drugs like Viḍanga (Embelia ribes Burm.f.), is substituted with fruits having similar appearance, like Embelia tsjeriam-cottam A.DC. ( Mentioned as a substitute by AFI, 2003) and Myrsine africana L. in trade but are not supported by Ayurvedic literature (Venkatasubramanian et al., 2013). The Ayurvedic Formulary of India mentions substitutes
for some of the herbs, but most of the suggestions appear to be based on trade practices and not taken from Ayurvedic literature. No logic or explanation is mentioned in AFI to substantiate the substitutes mentioned (AFI, 2000; AFI, 2003). The Ayurvedic Pharmacopoeia of India (API, 2001a) does not suggest substitutions.

Ayurvedic literature or trade practices on substitution are not backed by detailed Ayurvedic logic or scientific basis, to form a crystallized opinion on the legitimacy of the practices. However, even a cursory glance at the APDs mentioned in classical Ayurveda texts excites the scientific curiosity concerning the Ayurvedic principle behind selection of substitute drug. Some of the APDs suggested for ADs appear to be logical. E.g., Kuṣṭa (Saussurea lappa C.B. Clark) as a substitute for Puṣkaramūla (Inula racemosa Hook.f.) (Sastry, 2007). Here both the species belong to the Asteraceae family and are morphologically similar. They also have similarities in some of the chemical constituents. Both contain the biologically significant α-methylene γ-lactone (Gupta et al., 2006). But in other instances the APDs suggested do not show any apparent similarities with the ADs in terms of morphology, botanical lineage or chemical constituents. E.g., substitution of heart-wood of Rakthachandana (Pterocarpus santalinus L.) with the root of Uśīra (Vetiveria zizanioides L.) (Sastry, 2002). Pterocarpus santalinus is rich in phenolics and flavonoids (Arunakumara et al., 2011), whereas Vetiveria zizanioides contains mainly terpenoids (Bhushan et al., 2013).

1.7 Need for the study

Detailed scientific study of AD and APD is important mainly for two reasons:

(i) To identify the legitimate substitutes for unavailable/endangered medicinal plants drugs in contemporary times
(ii) To understand the fundamental Ayurvedic principles behind APD identification, so that one can proactively apply these in the future discovery of new medicinal plants and therapeutic functions

Legitimate substitutes for the endangered species, based on Ayurvedic suggestion and backed by the scientific studies may not only help avoid adulteration in the herbal drug industry, but also augment conservation efforts of endangered medicinal species like the *Aṣṭavarga* group by weaning away from threatened species. Scientific evidence for APDs may be required for pharmacopoeias to recommend substitution.

### 1.8 Objectives of the study

The overall aim of the study is to understand the Ayurvedic logic behind selection of *Abhāva Pratīnidhi Dravyas* (APDs- substitute herbs). A trans-disciplinary research (TDR) strategy involving Ayurveda, phytochemistry and pharmacology has been adopted to explore the possible logical relationship between ADs and APDs. A Trans-disciplinary research is designed to cross boundaries between scientific disciplines and between science and other societal fields and to include deliberation about facts, practices and values, in order to address a contemporary societal problem.

The objectives of this study were

1. **List of APDs:** To compile a list of substitutes from Ayurvedic texts between 14th to 19th century CE and tradition.

2. **Logic of APD concept:** To study the relationship between a selected list of the AD and APDs based on Ayurvedic principles and traditional practices

3. **Legitimacy behind substitution:** To use phytochemistry and pharmacology to evaluate the legitimacy behind substitution of selected AD-APD pairs

4. **Awareness on the use of APD:** To enhance the awareness on possibility of use of APD concept among Ayurvedic and traditional practitioners
1.9 Thesis overview

It was hypothesised that Ayurveda analysis and phytochemical-pharmacological studies of selected APD pairs will bring sufficient clarity to the concept and help to understand logic behind the same. Providing sufficient clarity and scientific proofs can convince regulatory authorities, industry and other stakeholders on legitimate substitution.

Chapter 2- Review of literature: introduces the Ayurveda, local health tradition and modern bio-medicine perspectives on APD concept. This is followed by a literature review on the studied species.

Chapter 3- Methodology: describes the overall trans-disciplinary research (TDR) approach followed for APD study.

Chapter 4- Systematic compilation of ADs and APDs from Ayurveda literature and traditional practices: This chapter compiles APDs mentioned in Ayurvedic literature and prevalent in living traditions. It also describes the method followed to prioritize list of 20 pairs of APDs for further studies.

Chapter 5- Analysis of 20 selected pairs of AD and APDs: In this chapter, the logical relationship between 20 selected pairs of AD-APDs has been provided as per Ayurveda.

Chapter 6- Phytochemistry of two selected AD-APD pairs: This chapter describes about the collection, primary processing, sensorial characters and phytochemical studies of two pairs of APDs viz., Ativiṣā (Aconitum heterophyllum) - Mustā (Cyperus rotundus) and Dāḍima (Punica granatum) - Vṛkṣāmla (Garcinia indica).

Chapter 7- Pharmacological evaluation of Ativiṣā and Mustā: This chapter analysis the jwarahara (antipyretic), atisāraghna (antidiarrhoeal) and medohara (antihyperlipidemic) actions of Ativiṣā (A. heterophyllum) and Mustā (C. rotundus).
Chapter 8 - *Agnivardhana action of Dāḍima and Vṛkṣāmla*: This chapter explains about the studies undertaken to evaluate and compare the *agnivardhana* action, with reference to enhancement of iron bioavailability by *Dāḍima* and *Vṛkṣāmla* in *in vitro* models.

Chapter 9 - **Conclusion**: Provides overall summary and future directions for research on APD concept.