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A REVIEW ON TRADITIONAL MEDICINAL PLANTS USED AS ANTIDOTES IN THE TREATMENT OF SNAKE BITES IN INDIA

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Keywords:

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ABSTRACT: Envenoming and deaths resulting from snakebites are particularly important public health problems in the rural tropics. Snake envenomation is included since 2009 in the World Health Organization (WHO) list of Neglected Tropical Diseases, as this condition remains largely neglected by national and international health authorities. The only available specific treatment is antivenom therapy, which consists of a pool of neutralizing immunoglobulins purified from the plasma of animals that are hyperimmunized against snake venom and specific toxins. However, the antivenom has some limitations, such as the poor ability to treat local effects, risk of immunological reactions, high cost, and difficult access in some regions. Therefore, the search for complementary therapies to treat snakebites is relevant, and the use of medicinal plants against snakebites is a historical practice throughout human history, and this knowledge has been transferred among the rural communities from generation to generation. Though tribal groups, forest dwellers, and rural people possess unique knowledge about plants and their uses, they are dwindling in number, and the younger generation is not interested in carrying on this tradition of folklore remedies. Hence, there is a grave danger of the disappearance of traditional knowledge. Therefore, it becomes the responsibility of the scientific community to unravel the information and to document the folklore remedies for availability to the whole world for the benefit of human beings to treat snake envenomation. In the present review, an attempt was made to enlist the variety of plant species from earlier research studies, which were shown to possess antivenom activity in snake bites in different parts of India, including certain tribal areas.

INTRODUCTION: Snakebite is a serious public health problem in many regions around the world, particularly in Africa, Asia, Latin America, and parts of Oceania¹. Conservative data indicate that there are between 1.2 and 5.5 million snakebites worldwide every year, leading to 25,000 to 125,000 deaths 2 .



Snake envenomation is included since 2009 in the World Health Organization (WHO) list of Neglected Tropical Diseases ³ (NTDs), as this condition remains largely neglected by national and international health authorities, funding agencies, pharmaceutical companies, etc.

Envenoming and deaths resulting from snakebites are particularly important public health problems in the rural tropics. The population in these regions experience high morbidity and mortality because of poor access to health services, which are often suboptimal ^{3, 4}. Snakes with major clinical importance belong to the families Elapidae (African and Asian cobras, Asian Kraits, African mambas, American coral snakes, and sea snakes) and Viperidae (old World vipers, American rattlesnake, and pit vipers, and Asian pit vipers)⁵.

Anatomy: The typical Snake-venom apparatus consists of paired venom glands, one on each side of the head below and behind the eye connected by ducts to hollow anterior maxillary teeth. In Viperidae, these teeth are large mobile fangs that retract against the roof of the mouth when the animal is at rest. In Elapidaes and sea snakes, the fangs are only slightly enlarged and fixed in an erect position. Vipers are characterized by somewhat triangular heads, elliptical pupils, enlarged maxillary fangs. After the production of the venom in the glands, it is injected in the victim via tubular and channeled fangs ⁶.



FIG. 1: ANATOMY OF SNAKE'S MOUTH

Snake Venom Composition: Biochemically, venoms are complex mixtures of pharmacologically active proteins and polypeptides, acting in concert to help in immobilizing the prey ⁷. The most common toxins in snake venoms are snake venom metalloproteinases (SVMPs), phospholipases A_2 (PLsA₂), snake venom serine proteinases (SVSPs), acetylcholinesterase (AChE), L-amino acid oxidases (LAAOs), nucleotidases and snake venom hyaluronidases (SVHs)⁷.

Clinical Manifestations of Snake Envenomation:

- Immediate and prominent local tissue damage (including myonecrosis, dermonecrosis, hemorrhage, and edema),
- Coagulation disorders (consumption coagulopathy and spontaneous systemic bleeding),

- Cardiovascular alterations (hypotension, hypovolemic shock and myocardial damage),
- Renal alterations (which could evolve into acute kidney injury),
- Neurotoxic action (descending paralysis, progressing from ptosis and external ophthalmoplegia to bulbar, respiratory muscle and total flaccid paralysis),
- Generalized rhabdomyolysis with myoglobinuria,
- > Intravascular hemolysis 5, 8.

Treatment: Only available specific treatment is the antivenom serum therapy, which consists of a pool of neutralizing immunoglobulins or immunoglobulin fragments, purified from the plasma of animals that are hyperimmunized against snake venom and specific toxins. Its effectiveness consists in its ability to provide to the patient antibodies with a high affinity to venom, aiming to eliminate the toxins responsible for the toxicity of envenoming, mitigating the progress of toxic effects induced by snake venom components⁹. However, the antivenom has some limitations, such as the poor ability to treat local effects, risk of immunological reactions, high cost, and difficult access in some regions^{8, 9, 10}.

If antivenom administration is initiated rapidly after envenomation, neutralization of systemic effects is successfully; usually achieved however. neutralization of local tissue damage is more difficult ⁸. Furthermore, the availability and accessibility of antivenoms are limited in many regions, such as Sub-Saharan Africa, Asia, and, to a lesser extent, Latin America. Thus this inability to treat local effects, as well as the increased time between accident and treatment, is the main reason for the temporary or permanent disability observed in many victims, which can lead to serious, social, economic, and health negative impact, given that most victim lives in rural areas 3 .

In this context, the search for complementary therapies to treat snakebites is relevant, and medicinal plants could be highlighted as a rich source of natural inhibitors and pharmacologically active compounds ^{6, 11, 12, 13}. There are several reports of the popular use of medicinal plants against snakebites around the world, especially in tropical and subtropical regions such as Asia,

Africa, and South America^{14, 15}. The rural and tribal people living in remote areas greatly depend on folk medicines for the treatment of bites from any venomous creatures¹⁶. The use of medicinal plants against snakebites is a historical practice throughout human history, and this knowledge has been transferred among the rural communities from generation after generation¹⁷. Nowadays, these herbal antidotes used in traditional folk medicine gained much attention by toxicologists worldwide as a tool for the design of potent inhibitors against snake venom toxins neutralize a broad spectrum of toxins, including the local tissue damage^{12, 15, 16, 17}.

Botanical families were found containing plants with a reputation against snakebites, among which the most cited ones were the families Fabaceae, Asteraceae, Apocynaceae, Lamiaceae, Rubiaceae, Euphorbiaceae, Araceae, Malvaceae, and Acanthaceae¹⁸. Medicinal plants with a reputation against snakebites are found all over the world, especially in tropical or subtropical regions of Asia, Americas, and Africa. This fact may be associated with richness of flora of these regions, as well as with the relative need of complementary therapies to treat snakebites, considering geographical features that could limit the distribution and availability of the antivenoms in these areas. As observed in, leaves and roots are the parts of plants most used in folk medicine. Regarding the mode of use, the most frequent one is the topical application of the vegetal products directly on the place of the bite. This is interesting, especially in snake venoms, that cause serious local tissue damage, such as Bothrops and Daboia species.

Since these snakes produce intense local tissue damage, which has a very rapid onset, a topical treatment could be interesting for a rapid inhibitory action ¹⁸. In a cross-cultural comparison of medicinal floras used against snakebites, Molander

et al., identified five countries with a high number of antiophidic plants and representing different cultures, geography, and floristic zones: Brazil, Nicaragua, Nepal, China, and South Africa. From these countries, some "hot" families were identified, which were Apocynaceae, Lamiaceae, Rubiaceae, and Zingiberaceae¹⁹.

In this article, an attempt was made to enlist the variety of plant species from earlier research studies, which were shown to possess antivenom activity in different parts of India, including certain tribal areas. It is important to emphasize that these plant species, in addition to their use as antiophidic agents, present a series of another popular use (data not shown) in popular medicine, mainly anti-inflammatory activity ²⁰. For example, *Jatropha gossypiifolia* (Euphorbiaceae) has antiophidic, anti-inflammatory, analgesic, antipyretic, healing, and anti-hemorrhagic uses, among others ²⁰.

Anti Venom Activities of Medicinal Plants of India Against Snake Venom Induced Local Tissue Damage: The plant families with most vegetal species showing positive results in antiophidic tests were Fabaceae, Euphorbiaceae, Apocynaceae, Lamiaceae, Asteraceae, Malvaceae, Melastomaceae, and Sapindaceae²¹. Crossing the data of popular use and of positive activity, we can highlight these families as "hot" ones, that is, families that might be preferred or prioritized in studies searching for antiophidic plants²¹. Snakes from the genus Naja, Bothrops, and Bitis were the most evaluated ones in these antiophidic assays 21 . However, although Naja and Bitis comprise a large fraction of the studies, virtually most of them are only *in-vitro* studies, dealing with the in vitro enzymatic inhibition of classes of venom toxins relevant to local tissue damage, such as phospholipases A_2 (PLsA₂), hyaluronidases (SVHs), and proteases 21 .

 TABLE 1: LIST OF MEDICINAL PLANTS WITH THEIR PARTS USED AGAINST SNAKE BITES IN DIFFERENT

 STATES OF INDIA

Plant Name	Parts Used	Use	References
Andrographis echiodes	Shoot	ND	22
Bryophyllum pinnatum (syn. Kalanchoe pinnata	leaf	Ι	23
Andrographis paniculata	Leaf, whole plant	I, E	16
Barleria cristata	Leaf, root, seed, whole plant	E	22
Blepharis maderaspatensis	Leaf	Ι	21
Connarus favosus	Bark	Ι	24
Capsicum annuum (syn. Capsicum frutescens)	Fruit, Root	I, E	22
Hygrophila auriculata	Seed	Ι	25

International Journal of Pharmaceutical Sciences and Research

Justicia adhatoda	Flower, leaf, root	I, E	16
Justicia japonica	Leaf	Ι	25
Rhinacanthus nasutus	Leaf, root	I, E	21
Verbascum Thapsus Selaginellaceae	Leaf	ND	26
Naringi crenulata	Fruit	ND	22
Aerva lanata	Rhizome	I	27
Amananthus blitum	Rinzonie	T	27
Amaraninus billum			28
Amarantnus spinosus	Lear, root, stem, whole plant	E	22
Amaranthus viridis	Leaf, stem, whole plant	E	17
Cyathula tomentosa	Leaf	ND	22
Allium cepa	Bulb, latex, leaf	E	27
Anacardium <i>occidentale</i>	Bark, fruit, leaf, root	I, E	29
Glycosmis pentaphylla	Leaf	I, E	16
Pistacia chinensis subsp. integerrima	Gall, leaf	E	22
Semecarnus anacardium	Root	T	27
Annona sauamosa	Bark fruit	IF	25
Calotronis gigantea	Latax loaf root	I, L I E	16
Culoiropis gigunieu	Elawar later last most short		10
Calotropis procera	Flower, latex, leal, root, shoot	I, E	28
Cryptolepis dubia	Root	ND	22
(syn. Cryptolepis buchanani)			
Cynanchum viminale (syn. Sarcostemma	Whole plant	E	30
viminale)			
Dregea volubilis (syn. Wattakaka volubilis)	Root	I, E	25
Gymnema sylvestre	Leaf. root	Ι. Ε	22
Pergularia daemia	Leaf	I, L	22
Rauvolfia serpentina	Flower leaf rhizome root seed	IF	31
Rauvolfia tetrankulla (sun Pauvolfia egneseens)	Prover, rear, filizonic, root, seed	г, L Б	16
The loss in discussion (Syn. Kauvoijia canescens)	KUUL		10
Tylophora indica	Leaf		25
Tylophora longifolia	Flower, leaf	ND	27
Vincetoxicum hirundinaria	Root	ND	22
Wrightia arborea	Bark	ND	22
Wrightia tinctoria	Leaf	ND	30
Cheilocostus specious	Bulb, Leaf, Tuber	I,E	22
Anaphyllum beddomei	Rhizome	E	16
Arisaema concinnum	Fruit tuber	ND	22
Arisaema jacauemontij	Flower leaf tuber	ND	22
Arisaoma tortuosum	Bulk tuber	I	32
	Loof tuber	I	22
Sauromatum venosum	Leal, tuber		52 22
Aristolochia <i>bracteolata</i>	Fruit, lear, whole plant	1, E 1 - E	32
Aristolochia indica	Leaf, root, whole plant	I, E	27
Aristolochia tagala	Whole plant	I, E	16
Thottea siliquosa	Leaf, root	E	16
Drimia indica (syn. Urginea indica)	Bulb	E	28
Sansevieria roxburghiana	Rhizome	Ι	25
Achillea millefolium	Whole plant	Ι	27
Ageratum convzoide	Flower, leaf, root	Е	33
Artemisia scoparia	Whole plant	E	34
Raubinia divaricata	Bark flower loof		3 4 22
	Dark, nower, lear		22
Blaens biternata			28
Bauhinia purpurea	Bark, Floer, Leaf	I, E	22
Emilia sonchifolia	Leaf, whole plant	I, E	16
Helianthus annuus	Seed	E	27
Betula alnoides	Bark, leaf	ND	22
Wedelia calendulacea	Leaf	Ι	27
Betula alnoides	Bark, leaf	ND	22
Wedelia calendulacea	Leaf	Ι	27
Tricholenis olaberrima	Root	ND	22
Saussuraa simpsoniana	Flower	ND	22
Divelage indige	Flower socd	IE	22
	Tiowei, seeu	1, E	21
Pentanema indicum	Leaf, root	1	25

International Journal of Pharmaceutical Sciences and Research

Cynoglossum zeylanicum	Root	Ι	35	
Ehretia microphylla (syn. Ehretia buxifolia)	Root	I, E	27	
Trichodesma zeylanicum	Root	I, E	27	
Brassica rapa (syn. Brassica campestris)	ND	E	28	
Boswellia serrata	Bark	Ι	33	
Opuntia ficus-indica (syn. Opuntia vulgaris)	Root	ND	28	
Cannabis sativa,	ND	Ι	34	
Carica papaya	Fruit	ND	36	
Ipomoea pes-tigridis	Root	I, E	33	
Evolvulus alsinoides	Root	Ι	25	
Argyreia nervosa (syn. Argyreia speciosa)	Root, seed	ND	22	

I = Internal use, E = External use, ND = Not defined

Medicinal Plants Used by Tribal people in some parts of India:

1. Medicinal Plants Used by the Tribal People of Kolli Hills of Tamil Nadu: The knowledge of medicinal plants has been accumulated from different medicinal systems such as Ayurveda, Unani, and Siddha. In India, it is reported that traditional healers use 2,500 plant species and 100 species of plants serve as a regular source of medicine. Eastern Ghats of India is ethnobotanical, very rich in having a wide variety of medicinal Traditional medicinal knowledge plants. is important not only for its potential contribution to drug development and market values but also for the healthcare professionals²¹. Documenting the indigenous knowledge through ethnobotanical studies is important for the conservation and utilization of biological resources ²¹. Tribal groups, forest dwellers and rural people possess unique knowledge about plants and their uses ²².

Although many studies are there concerning the ethnobotanical investigation of common ailments such as cuts, wounds, cold, cough, fever, asthma,

chronic disorders, ulcer, leprosy, rheumatism, there is scarce information on the folk remedies for snakebite²⁴. Therefore, some studies in search of antidotes in poisonous bites and veterinary diseases have been carried out targeting the Kolli Hills²³. Eastern Ghats of India is ethnobotanically very rich in having a wide variety of medicinal plants. With its diverse topographical condition, this region is well suited for a range of medicinal plant species. Eastern Ghats of Kolli Hills are situated in the Namakkal District of Tamil Nadu with an area of 441.8 sq. km. Besides this, it is made known that the traditional healers are dwindling in number; the younger generation is not interested in carrying on this tradition of folklore remedies. Hence there is a grave danger of the disappearance of traditional knowledge²¹. Therefore, it becomes the responsibility of the scientific community to unravel the information and to document the folklore remedies for availability to the whole world for the benefit of human beings²¹. In view of this, medicinal plants that are used in the treatment for the snake bite by the tribal people of Kolli hills are tabulated below.

TABLE 2: LIST OF MEDICINAL PLANTS USED BY THE TRIBAL PEOPLE OF KOLLI HILLS OF TAMIL NADU FOR SNAKE BITES

Botanical	Vernacular	Family	Useful	Preparations & mode of
name	name		parts	application
Abrus precatorius L.	Kundumani	Fabaceae	Roots, Leaves	Paste (internal & external)
Achyranthes aspera L.	Naaiuruvi	Amaranthaceae	Whole plant	Decoction (internal)
Anisomeles malabarica R.Br.	Peimiratti	Lamiaceae	Whole plant	Paste (internal)
Aristolochia indica L.	Urikakodi	Aristolochiaceae	Whole plant	Paste (external)
Azadirachta indica A. Juss.	Vembu	Meliaceae	Flowers	Juice (internal)
Blepharis maderaspatensis L.	Naikalli	Acanthaceae	Leaves	Juice (internal)
Calendula officinalis L.	Marikollundu	Asteraceae	Flowers	Juice (internal)
Calotropis gigantea L. R. Br.	Erukku	Asclepiadiaceae	Roots	Paste (internal & external)
Cardiospermum helicacabum L.	Mudakothan	Sapindaceae	Leaves	Paste (external)
Cassia alata L.	Semaiagatti	Caesalpiniaceae	Leaves	Paste (internal)
Cassia tora L.	Tagarai	Caesalpiniaceae	Seeds	Decoction (internal)
Citrus limon L.	Elumichai	Rutaceae	Fruits	Paste (external)
Curcuma angustifolia Roxb.	Kattumanchal	Zingiberaceae	Rhizome	Paste (external)
Cyperus rotundus L.	Koraipul	Cyperaceae	Roots	Paste (external)

International Journal of Pharmaceutical Sciences and Research

Medicinal Plants Used by the Tribal People of Arakuvalley Mandalam, Visakhapatnam District, Andhra Pradesh, India for Snake Bite: The use of plants by man is as old as the human civilization itself. The term Ethnobotany refers to the interrelationship between the primitive people and plants growing around them. The primitive people were devoid of any written language but retained their tradition by verbal means. The consistent curiosity of early man had led him to the systematic observation of plants, which had influenced not only his life but the mode of his living as well.

According to WHO ²⁵, 80 percent of the world population depends upon traditional medicine for their primary healthcare needs. Folk remedies

consisting of simple methods of treatment developed by trial and error over a long period hold an important place in almost all societies. The indigenous knowledge and practices of the tribes on the utilization of plant resources as medicine should be reported and preserved before they get lost due to increasing integration.

Araku Valley is a hill station and a Mandal in Visakhapatnam district in the state of Andhra Pradesh in India. It has got an amazing nature with thick forests surrounded all over. Araku is popular for its world-famous coffee plantations. Following are the list of the plants ²⁶ useful for the treatment of snakebite by the different tribal people of Visakhapatnam District, Andhra Pradesh, India.

 TABLE 3: LIST OF MEDICINAL PLANTS USED BY THE TRIBAL PEOPLE OF ARAKUVALLEY MANDALAM,

 VISAKHAPATNAM DISTRICT, ANDHRA PRADESH FOR SNAKE BITES

Name of the plant	Family	Vernacular name	Mode of administration
Acampe carinata (Griff.)	Orchidaceae	Kano- Kato	The root paste is applied externally on scorpion
Panig.			and snake bites
Arisaema tortuosum	Araceae	Gandana	Tuberous root is ground into paste and one spoon
(Wall.) Schott.			of it is administered orally and a portion of it
			applied on the bitten area For snake bite
Caladium bicolor Vent.	Araceae	Rudra chama	Quarter cup of tuber juice is given and a portion of
			it is applied on the bitten area immediately after
			bite for snake bite

3. Medicinal Plants Used by the Konda Dora Tribes, Visakhapatnam District, Andhra Pradesh, India for Snake Bite: The Konda Doras are found chiefly in the scheduled areas of Visakhapatnam District of Andhra Pradesh. They call themselves as Kubing or Kondargi in their own dialect, which is called Kubi. Konda Doras living in Visakhapatnam can speak adivasi Oriya and Telugu. Konda Dora tribe is divided into a number of clans such as Korra, Killo, Swabi, Ontalu, Kmud, Pangi, Paralek, Mandelek, Bidaka, Somelunger, Surrek, Goolorigune olijukula etc.,. The following are the list of the plants ²⁷ useful for the treatment of snakebite by Konda Dora Tribes, Visakhapatnam District, Andhra Pradesh, India.

TABLE 4: LIST OF MEDICINAL PLANTS USED BY THE KONDA DORA TRIBES, VISAKHAPATNAMDISTRICT, ANDHRA PRADESH FOR SNAKE BITES

Botanical name	Family	Vernacular name	Habit	Mode of administration & Dosage
Butea superba Roxb.	Fabaceae	Palasamu	Tree	Flowers are ground with the leaves of Cinnamomum
				zeylanicum and the paste is administered twice a
				day orally
Caladium bicolor	Araceae	Rudra chama	Herb	Quarter cup of tuber juice is given and a portion of
Vent.				it is applied on the bitten area immediately after bite
Wattakaka volubilis	Asclepiadaceae	Palateega	Climber	A handful of tender leaves are crushed and eaten to
(Linn. f.) Stapf.				get vomiting and also acts as an antidote

4. Medicinal Plants Used by the Tribal Communities of Salugu Panchayati of Paderu Mandalam, Visakhapatnam, District, Andhra Pradesh, India for Snake Bite: An important prerequisite for proper utilization of raw materials of the country is the survey of its natural resources and the preparation of an inventory. It is necessary that we should have full knowledge regarding the occurrence, frequency, distribution, and phenology of various plants for their proper utilization. Following are the list of the plants ²⁸ useful for the treatment of snakebite by the different tribal people of Salugu Panchayati of Paderu Mandalam, Visakhapatnam, District, Andhra Pradesh, India.

Salugu Panchayat is an interior pocket of the Paderu Mandal. The altitude in this region ranges from 600 to 900 m. The panchayat consists of 24 villages and hamlets belonging to different tribal groups like the Bagata, Valmiki, Nookadoras, Kondadoras, Konda Kammaras, and Khonds. The total population of the panchayat is 2,500. Apart from paddy, agriculture is primarily on dry land. Minor cereals, millets, pulses, red gram, and oilseeds like niger and castor, are the main cash crops. Shifting cultivation is widely practiced in this panchayat.

 TABLE 5: LIST OF MEDICINAL PLANTS USED BY THE TRIBAL COMMUNITIES OF SALUGU PANCHAYATI

 OF PADERU MANDALAM, VISAKHAPATNAM, DISTRICT, ANDHRA PRADESH FOR SNAKE BITES

Botanical name	Family	Vernacular name	Habit	Useful Parts
Actinopteris radiata (Swartz) Link.	Actinopteridaceae	Mayurasikha	Herb	Root
Caladium bicolor Vent.	Araceae	Rudra chama	Herb	Tuber
Crotalaria laburnifolia Linn.	Fabaceae	Pedda giligicha	Shrub	Root

6. Medicinal Plants Used by the Valmikis of Visakhapatnam District, Andhra Pradesh, India for Snake Bite: According to 1991 census, the tribal population in the State was 41.99 lakhs. Of these 42,944 Valmikis are living in the agency tracts of Visakhapatnam district. Valmikis are agriculturists and now became laborers. Some of them become traders and petty money lenders. They practice Podu cultivation on the slopes of hills. Interviewing traditional healers for accurate information about medicinal recipes, their

component herbs, and their medicinal uses constitutes an important activity in the ethnopharmacological field investigation.

The knowledge and experience of a traditional healer is considered valuable as it comes from thousands of years of trial and error and forms the basis of modern medicine and therapeutics ²⁹. The ethnobotanical information of Valmikis is poorly known. The following is the one popular medicinal plant used by the Valmikis.

 TABLE 6: POPULAR MEDICINAL PLANT USED BY THE VALMIKIS OF VISAKHAPATNAM DISTRICT,

 ANDHRA PRADESH FOR SNAKE BITES

miy vernacular n	ame Habit	Mode of administration & dosage
rbiaceae Kokkera tig	ga Tree	10-12 g of root bark extract administered
		twice in an hour
)	prbiaceae Kokkera tig	rbiaceae Kokkera tiga Tree

CONCLUSION: Medicinal plants are safe; however, the toxicity of these plants should be studied before consumption. This review of ethnomedicinal information regarding the traditional medicinal plants throughout India, including different tribal areas, may be helpful for the treatment of snake bites.

Only a few people are practicing with a little knowledge that was transmitted orally from their elders. Snakebite is a more common and many times potentially fatal phenomenon. Anti-snake venom being the only therapeutic option available, but having many drawbacks, herbal plants provide a solid platform for the natural treatment of this serious issue.

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International Journal of Pharmaceutical Sciences and Research

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