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Evolution of "*Agadatantra*"- Forensic Medicine and Toxicology of Indian System of Medicine: A Review

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ABSTRACT

BACKGROUND: With the evolution of Indian civilization and its development, Agadatantra came to light as one of the eight branches of Ayurveda, the Indian system of medicinedisciplined and has evolved a lot over the years. Agadatantra mainly deals with the toxicological aspect ofAyurveda and code of conducts relevant to the field of medical practices including Ayurveda professional medical ethics and duty of Ayurveda physician towards patient and state. The related subject matter is abundant in Charaksamhita, sushrutasamhita, AstangaSamgraha, Astangahrdyam and kautilyaarthashastra mainly. Forensic Medicine and toxicology is part of Ayurveda Undergraduate and Postgraduate studies as AgadaTantra Vyavahara Ayurveda evum Vidhivaidyaka.

OBJECTIVE: To evaluate the evolution of Agadatantra over the years.

METHODS: Literature review of relevant classical text books and published journals.

CONCLUSION: Development of Agadatantra was very impressive till early part of 15th century, it then slowed down. However, there has been remarkable progress in Ayurveda and AgadaTantra after the 1970.

KEYWORDS

ADR; Schedule E Drug; Antidote; Visha; Agada

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INTRODUCTION

"We can never be fully in possession of a science until we know the history of its development"

-CHARLES GREENE CUMSTON

The history [Table-1] of forensic medicine is the key to past; explanation of of British domination[1].

present.Forensic medicine and toxicology of present India has attained its current state of development by passing through several phases. Lately it has accepted the western system of medical discipline because of British domination[1].

Table 1 List of major events in history W.S.R development of to Forensic Medicine and Toxicology in India

No	Time period	Event
1	16000 BC	Hunter used aconite poison to kill animal in Kenya.
2	Indus valley civilization (3250 -2000 BC)	Orpiment and *Aconitum napellus* was used for assassination.
3	3102 BC	Manu prescribed punishment for poisoning, infanticide and illegal abortion.
4	3100 -3000 BC	People in Egypt used poisoned arrows.
5	2737 BC	Marijuana was used to treat gout in China.
6	2000 BC	Chinese Emperor Shen Nung experimented with poisons.
7	1600 BC	The Smith Papyrus cites the use of charms against snake poison[2].
8	1200-900 BC	Atharva Veda mentions the use of poisoned arrows in war. Sthavaravisha(Irritant plant toxin) were mentioned as the major source of poisoning[3].
9	Seventh Century BC	Father of Indian medicine Charaka discovered a number of antitoxic formulations; snake envenomation antidote; acute and chronic alcohol intoxication; use of emesis and purgation for reducing the absorption of poison. He used lower grade animal for experimental toxicology.
10	Sixth century BC	The Indian physician Kashyap was able to cure snakebite envenomation.
11	200-300AD	Father of Indian surgery Sushruta defined "Agadatantra", a term akin to the modern term ''Toxicology" and classification of poisons, antidotes, diagnostic touchstone of intoxication and medical ethics. He delineated Orpiment and realgar as metal poison.
12	460 BC	Hippocrates suggested managing poisoned patients by limiting the absorption of poison[4].
13	399 BC	Socrates was executed by hemlock (*Conium maculatum*) poison.
14	384–322 BC	Aristotle described the preparation and use of poisonous arrow.
15	350-275 BC	Indian philosopher Kautilya (chief advisor and Prime Minister of the Indian Emperor Chandragupta and professor of political science and economics at the University of Taxila) introduced fingerprint technique (Trija) and postmortem examination in case of death of all cases of poisoning, asphyxial death[5].
16	183 BC	Hannibal took his own life by taking cyanide.
17	132-63 BC	Mithridates VI developed antidote -"mithridatum."
18	54 AD	Locusta, one of the most famous prisoners of all time, was hired by Agrippina, Nero's mother, to poisonClaudius, her husband and Nero's stepfather, with poisonous mushrooms. Some versions assert that the poison used was arsenic[6].
19	55 AD	Locusta was murdered by soup containing arsenic.
20	Age of Arsenic (15 -18 Centuries)	Arsenic (Ideal homicidal poison) was the favorite choice of all assassination creeds because during this period there was no scientific test to detect arsenic poisoning.
21	1492–1541	Paracelsus (PhilippusAureolus Theophrastus Bombastus von Hohenheim)

		developed the experimental toxicology model.
22	1534	Pope Clement VII was assassinated with poisonous mushrooms
23	September 1613	Somerset murdered poet Sir ThomasOverbury in Tower of London.
24	1666	A number of American soldiers died in accidental poisoning with Thorn-apple (*Daturastramonium).*
25	1630-1676	Marquise de Brinvilliersmurdered her father, mother, brothers and more than 50 hospital patients by using arsenic.
26	14 August 1751	Mary Blandy murdered her father with arsenic.
27	1730-1805	FeliceFontana discovered snake venom glands and obtained snake venom, which he used for a variety of experimental toxicology with animals[7].
28	1769	Secundus designed out line of stomach pump
29	1773	Scheele discovered mechanism of poisons adsorption by charcoal.
30	1787-1853	Mathieu Orlifia(Father of Modern Toxicology) created new techniques and refined existing toxin analyzing techniques.
31	1794 – 1846	James Marsh invented the Marsh test for detecting arsenic.
32	1805	Philip Syng Physick ("The father of American surgery") used Secundus designed stomach pump for gastric lavage in a case of accidental opium poisoning.
33	1813	French chemist M.Bertrand discovered charcoal antidotal effect against arsenic trioxide.
34	1822-1827	India's first modern medicine medical college was established in Kolkata andthen in the year of 1827. 1st Ayurveda institution started in Government Sanskrit college Kolkata(India).
35	1836	First academic autopsy conducted in Kolkata by legendary surgeon Dr. Madhusudan Gupta resident of district Hooghly, state Bengal (India).
36	1840-1842	Henry Burton described clinical sign blue line on the gums (Burton line or Burtonian line) in chronic lead poisoning patients. Hugo Reinsch invented Reinsch's test to detect arsenic and its compoundsin the year of 1842.
37	1851	"The Arsenic Act" was passed by The United kingdom Parliament during the reign of Queen Victoria to regulate sell of arsenic and homicides.
38	1870	Adolf Lieben. Discovered iodoform test for alcohol. It is also called the Liebenhaloform reaction test.
39	1892-1897	Heam Chandra Bose and Azizul Haque developed fingerprint classification system with their supervisor Sir Edward Richard Henry in Kolkata (India) .The Henry Classification System, co-devised by Haque and Bose was accepted in England and Wales when the first United Kingdom Fingerprint Bureau was founded in Scotland Yard, the Metropolitan Police headquarters, London, in 1901[8].
40	1906	Nicloux prescribed the method of determination ethyl alcohol level in blood and urine with the photoelectric colorimeter[9].
41	1910	Russian botanist Mikhail Semyonovich Tsvet invented Chromatography;latter it was used for detection of poison.
42	1916-1956	2ndAyurveda medical college was established in Kolkata (India) in 1916 to teach "vishatantra" (toxicology) and Agada (Ayurvedic - antidote) first in the country. As per CCIM data-base the college known today by the name of "J.B.ROY state ayurvedic medical college" [10]. THE DRUGS AND COSMETICS ACT was passed in the year of 1940 in India. Methylmercury poisoning (Minamata disaster) in the year of 1956 at Japan.
43	1958	"Kerala food-poisoning tragedy" in India; more than 100 died; 1000 people were poisoned with parathion (parathion-ethyl).
44	1966-1968	Raman Raghav (serial killer) killed more than 41 victims in Mumbai; India.
45	1975-1976	Charles Sobhraj (The Bikini killer) murdered more than 10 victims in Thailand, Nepal, India, and Malaysia.

46	September 7, 1978	Georgi Markov was assassinated on a London street via a pellet containing Ricin[11].
47	1978	The cult leader of the Peoples Temple; Jim Jones led more than 900 followers in a mass suicide via cyanide. (Jonestown Massacre).
48	1984	Bhopal disaster or Bhopal gas tragedy occurred on the night of 2–3 December 1984 at the union carbide India limited (UCIL) pesticide plant in Bhopal, India. Over 500,000 people were exposed to Methyl Isocyanate gas and other chemicals. 3,787 deaths related to the gas release; the gas leak caused 558125 injuries, including 38,478 temporary partial injuries and approximately 3,900 severely and permanently disabling injuries. 8,000 died within two weeks, and another 8,000 or more have since died from gas-related diseases.
49	1994-1996	Establishment of the National poisons information center at the All India Institute of Medical Sciences, New Delhi in December, 1994. Sukhwinder Singh Dhillon murdered 5 victims for their insurance money with strychnine in India and Canada in 1995-1996.
50	1999-2007	Mallika also known as Cyanide Mallika, first Indian women serial killer, killed 6 women by using cyanide in Bangalore (India).

Table 2 Ancient Book of Indian Forensic Medicine and Toxicology

Book name	Chapter number	Sthana (parts)
Charakasamhita	23	Chikitsa
Sushrutasamhita	1-8	Kalpa
Astangasanghra	40-48	Uttaratantra
Astangahridaya	35-38	Uttaratantra
Kashyapasamhita	----------	Sarvavidhivishapratipadika
Haritasamhita	56	Truteeya
Bhavaprakash	67	Chikitsa
Bhaisajyaratnavali	----------	Visharogachikitsa
Rasatarangini	24	----------
Kouyilyaarthasasthra	1,2,3,4,11,12,13,14	----------
Vishavaidyajyotsnika	1-18	----------

AIMS AND OBJECTIVES

To evaluate the evolution of Agadatantra (Indian Forensic Medicine and Toxicology)

MATERIALS & METHODS

Conceptual study based on review of literature regarding Aadatantra (Indian Forensic Medicine and Toxicology) from all available literature, related web page and related research articles.

SEQUENTIAL DEVELOPMENT

Indus Valley Civilization (3250-2000 BC) –Indus valley civilization has been accepted by all that it is much more ancient than the written chronicles of Indian history. In this period metals and minerals like Arsenic; Sulphur; Mercury; Lead; Copper may have been used in melting and alloying process but it is just as likely that they were used for the purpose poisons ,medicine, weapons cosmetics and colorant[12].Gwen Robbins Schug study showed a plenty of evidence of injury caused by blunt force trauma[13]and gives idea about commonly used weapons like cudgel, long club for assassination and ancient skeletons give evidence for leprosy in India[14] and use of orpiment in its treatment purpose. During

this period metallic seals were used for controlling adulteration.

Manu (3102 BC) – Manu prescribed a wide number of rules & regulations for controlling criminal activity likely fixing age of marriages and punishment for offences like rape ,unnatural sexual offence ,abortion , infanticide ,abduction, adultery, intoxication, murder, early age marriages, injury .He directed how to record evidence in trial and disregard the evidences of drunk, insane, old and diseased subjects, children and weak minded individuals[15].

Charaka (Seventh Century BC)-Charaka the "Father of Indian medicine" drew the outline of "The code of conduct" for the medical practitioner to protect the community from malpractice and developed medical ethics. He described the social status for the physicians and gave guidelines regarding duty of aphysician in case of poisoning and diagnostic touchstone for early identification of poisoning cases. Charaka classified the poison on the basis of it origin i.e. -sthavara (poisonous plant) and jangama (poisonous animal like venomous snake, insect, venomous arachnids and other venomous creatures). He explained the 8 stages of poisoning with symptoms. Charaka highlighted "Garavisha" -a special type of poison –akin to artificial or mechanical poison which produces sub-acute and chronic toxicity[16],not only that he also described doosivisha(cumulative toxicity), Madatayaya (alcohol intoxication) ,medico legal importance of alchol[17],assault and injury by poisonous weapon[18],bee sting envenomation, spider, scorpion envenomation, rat bite, poisonous fish , frog and prescribed a large number of antitoxic and antioxidant herbo – mineral formulation for toxicological management .He prescribed 24 remedial measures[19] including first-aid measures ,eliminative therapy like –emesis, purgation, bloodletting, snuffling etc ; countering therapy - antidotes, antioxidant, antitoxic medication etc ;cardio protective therapy ;resuscitation therapy , symptomatic therapy. Charaka strongly recommended blood-letting therapy for removing toxin from the blood stream; it is one kind of haemofiltration technique to eliminate toxin from the human body and the ancient nashya(insufflations)-an aerosol nasal therapy, non –invasive delivery of drugs to the human brain. A study by Ramesh Raliya .et al (2017), showed that the nano particles of the nasal spray reached the brain within 30 minute and crossed the blood –brain –barriers.

Sushruta(1000-1500BC) -Father of Indian surgery Sushruta defined agadatantra, a term akin to the modern term

‘‘toxicology”. He defined “Agadatantra” as a special branch of Ayurveda which deals with the signs and symptom and also their detection and management of poisoning; resulting from the bite of snakes; arthropod and various other poisons produced by improper combinations of substances or drugs.Sushruta referred poison as “Visha” which caused languor of sprits[20]. He highlighted quantity, quality of poison; factors modifying actions of poisons, mode of administration of poison, toxicodynamic and toxicokinetics and also used lower grade animals for toxicological analysis[21]and detecting criteria for poisoned food and the poisoner[22]. Sushruta’s experiment of poison in animals can be comparing today’s experimental toxicology. He classified poison in to two type i.e., “Sthavaravisha” (Immobile irritant poison), “jangamavisha” (poison from mobile source).Sthavaravisha (Immobile irritant poison) are 55 in numbers [Table -3] .Sushruta included Arsenical compound haratal(Orpiment) in sthavaravisha (Immobile irritant poison) and described it as metal poison. Again he mentions 7 stages of symptom for immobile irritant poison and its stage wise treatment with antitoxic and antioxidant formulation; in jangamavisha (poison from mobile source) he include snake, insects, worms, spider rodents etc. and briefly described there envenomation sign symptom and respective treatment. Sushruta give more importance to snake bite envenomation. He described seven phase of envenomation and classified snake in fivefamilies on basis of morphological characteristics such as arrangement of lepidosis, dentition, and fang markslength, eye, sexual character and venom[23].These family’s are:

Darvikara[24]- This family includes 26 species .These snakes are hooded and fast-moving ,because of fast body movement they have ability of snapping bite, having marks of wheel, plough, auspicious cross and after bite these snakes’ venom attack the respiratory muscles and leads to paralysis of the muscles resulting into death due to respiratory arrest. These snakes can be correlated with Elapidae family snakes like cobra (Naja). Cobra can extend neck into a hood, there may be monocilate or binocilate marks(**Figure 1)** on the hood; this marks are similar to those described by Sushruta and has ability to fast movement and on envenomation, neurotoxin venom of cobra paralysesthe tongue ,inter-costal muscles, diaphragm, scalene muscles resulting paradoxical respiration at last death due to respiratory failure. ***Mandalini***[25, 26]- This family contains 22 species, big in length with

various circular sports in body and after bite; venom of these snakes vitiates the blood. These snakes can be correlated with viperdae families Russell's viper; because Russell's viper has heamotoxic venom , there are 3 rows of chained dark spots over the entire body(**Figure -2)** and growing up to several feet.

Rajimat[27, 28]–These snakes are glossy and marked with oblique and straight bands of various colours again rajimat subdivided in to 10 species. After envenomation, these produce stiffness of body, rigor, and vision disturbances with heaviness in head etc. These snakes can be correlated with elapidae families' kraits. In India commonly found kraits are *Bungaruscaeruleus* (Indian krait) and *Bungarusfasciatus*(Eastern part of India's krait or banded krait); because krait have most distinctive features like glistening broad bands of yellow, alternate with black, whitish bands, sometime grey or dark brown colour throughout the body(**Figure- 3)**; and have predominantly neurotoxic venom.

Nirvisha-These are non- poisonous snake; it is again dividedinto 12 species.

Vaikaranja-These snakes are basically cross breed of above families.

Sushruta also described cosmetic toxicity, dermatological manifestations, its management and "Dooshivisha" – concept of cumulative toxicity[29]and its treatment with "Dooshivishariagada"-an antitoxic formulation. Sushruta deals not only with theinjury[30], wound surgical procedure and its related clinical problem aspect but also prescribed guide line and moral principle for a physician that can be correlated with today's "Medical ethics". He wrote 8 separate chapters for toxicology and associated problems, complications of toxin and how to treat them. Sushruta mentioned a wide number of antidote, antitoxic, antioxidant formulations. The research work validates promising effect and potency of these formulations[31.] Sushruta identified air, water, land pollution as the causative factor for epidemic calamities and recommended formulation for purification of air, water[32].

Table 3 Sthavara Visha (Immobile Irritant Poison) Mentioned by Sushruta

Poison source	Number	Example
Root	8	*Abrusprecatorius*
Leaf	5	*Arisaema* species,*Tectonagrandis,Lagenariasiceraria*
Fruit	12	*Momordicadioca,coallocarpusepigaeus,vitexagunuscastus*
Flower	5	*Anthocephalusindicus*
Bark	7	*Piper nigrum*
Latex	3	*Euphorbia nerifolia*
Tuber	13	*Aconitum napellus*
Metal poison	2	Orpiment(Arsenic trisulphite)

Vaghbhat (3-5 AD)–Vaghbhat mentioned the mode of action of the poison; properties of poison, clinical symptom of suspected case of poisoning and critical period of poisoning and classified the poison on the basis of its origin in to two types (plant source and animal source) and based on nature of poison, divided into - natural poison, artificial or synthetic poison. This artificial poison is known as "Garavisha".This type of "garavisha" (artificial or synthetic poison) was prepared by mixing drugs with the opposite pharmacological actions. It kills the person either quickly or after some time or after a long period. This may be a type of dose related toxicity or adverse drug reaction or chronic toxicity. Vaghbhat described the features of assaults, injury by poisoned smeared weapons and suggested local wound area examination for tracings the poison[33]. He also gave elaborate explanation of the features of dog bite; hydrophobia and its acute and prophylaxis treatment. Vaghbhat introduced a large number antitoxic formulation for snakebite and arthropod envenomation.

Age of Herbo-mineral Formulation (800 AD) –Nagarjuna was the revolutionary man of India's metallic pharmacology. He described parada (mercury) as a nucleus of herbo-mineral formulation and he developed the concept of metal pharmacology, pharmacokinetics, biotransformation, pharmacodynamics, and therapeutic indication, adverse effect of heavy metal, and toxic effect of improperly prepared heavy metal and irritant plant formulation and also he described therapeutic modification, purification, molecular mass reduction procedure and adjuvant of heavy metals.Ayurvedic medication commonly use metals like Parada (mercury), Tamra (copper), Naga (lead), swarna (gold),lauha (iron), tin (vanga), yasada(zinc) etc.

Table 4 ADR and Antidote

Name	Therapeutic indicated dose (TID)	Adverse drugs reaction (ADR) and chronic toxicity	Antidote
Parada (mercury)	125mg/day	Dermatological-disorder, osteoarthritis, fainting, vomiting	• Dehydrated borax 250mgalong with clarified butter • Gandhak(sulphur) • *Corindrumsativum* with sugar candy • *Pipernigrum*with clarified butter • Gandhaka (Sulphur) with *Piper betel*
Tamra (copper)	15-60mg/day	Anorexia ,nausea, vomiting, colic pain, obesity, burning sensation, hallucination, death	• Dehydrated borax 250mg along with equal quantity clarified butter • *Corindrumsativum* with

			sugar candy
Naga (lead)	30 to 125mg/day	Diabetes mellitus ,emaciation, anemia , jaundice , Dermatological disorder, abdominal tumour, oedema, fistula in ano, dyspepsia	• Dehydrated borax250mg along with equal quantity clarified butter • Purified Swarnabhasma (Gold ash) mix with Haritaki (Termenilachebula) and sita (Sugar candy)
Vanga (tin)	125 - 250mg/day	Diabetes mellitus, Dermatological disorder, cardiovascular disease including dilated cardiomyopathy (DCM) ,colic pain in abdomen, hemorrhoids, gout, goiter , respiratory disease –specially cough and breathlessness ,vomiting	• Powder of *Gymnemaslylvestree*fruit with sugar candy • Dehydrated borax250mg along with equal quantity clarified butter
Swarna (gold)	15-30 mg/day	Weakness,impotency, irregularity incybernetics chain	• Dehydrated borax250mg along with equal quantity clarified butter • Fruit powder of *Terminaliachebula* with sugar candy.
Rajata(silver)	30-125 mg/day	Anaemia, itching, pyrexia, constipation, benign cervical lymphadenopathy, headache.	• Honey • Dehydrated borax250mg along with equal quantity clarified butter
Lauha (iron)	30-250 mg/day	Dilated cardiomyopathy with stable angina, Dermatological disorder, urolethiasis, colic pain, burning sensation, even death.	• Fruit powder of *Embeliaribes* with fresh extract of *Sesbaniagardiflora* leaves
Aconitum napellus	30-125 mg/day	Burning sensation, fainting, cardiac arrhythmia, cardio- respiratory failure.	• Dehydrated borax 250mg along with equal quantity clarified butter
Strychnosnuxvomica	30-125 mg/day	Convulsions, respiratory distress, epigastric pain ,even death	• Dehydratedborax 250mg along with equal quantity clarified butter
Opium	30-125 mg/day (for non opium addicted person)	Hallucination,drowsiness, fatigue	• Dehydrated borax250 mg along with equal quantity clarified butter
Croton tiglium	15-30 mg/day	Burning sensation in abdomen (due to gastro-intestinal irritation) vomiting ,diarrhea	• Dehydrated borax 250mg along with equal quantity clarified butter
Thorn apple (Datura)	15-62 mg/day	Restlessness, dryness in mouth, cardio- respiratory failure.	• Dehydrated borax 250 mg along with equal quantity clarified butter • Patient should be made to vomit by using*Randiadumetorum* • Drink Milk with added sugar
Cannabis Indica	250-500 mg/day (for non addicted person)	Hallucination,drowsiness,psychosis	• Cow curd mix with Ginger *(Zingiberofficinale)* along with fresh root extract of *poincianticelata*

			• Dehydrated borax 250 mg along with equal quantity clarified butter
Abrusprecatorius	65-125 mg/day	cardiomyopathy with stable angina	• Dehydrated borax 250 mg along with equal quantity clarified butter
Semecarpusanacardum	125-375 mg/day	Hyper melanin pigmentation on locally application, burning sensation in abdomen.	• *Ameranthustricolor* extract with clarified butter for external application • Dehydrated borax 250 mg along with equal quantity clarified butter orally
Oleander	Base-on patient body mass index	Mainly cardiac abnormality features with delirium ,dizziness ,drowsiness, seizures ,even death	Symptomatic treatment
Calotropis	Base-on patient body mass index	Vomiting ,pain abdomen , seizures even death; on prolong skin application lead to blister formation	Symptomatic treatment
Zingiberofficinale	Base-on patient body mass index	Burning sensation in stomach	Symptomatic treatment
Haratal/AS_2S_3	15-30 mg	Alopecia , hypoglycemia, renal calculi, cardiomyopathy , even death	*Carumcarvi*with Sugar candy Dehydrated borax 250 mg along with equal quantity clarified butter orally
Gauripashana (White arsenic)	15-30 mg	renal calculi, nephrotoxicity, prostatic hyperplasia,difficulty in micturation	Dehydrated borax 250 mg along with equal quantity clarified butter orally. Cow milk with honey

Buddha era (4th-5th century) - Buddhism was propounded by prince Siddhartha Gautama [Gautam Buddha] in 4th -5th century BC born at Lumbini; southern part of Nepal.GautamBuddhawas not only a philosopher but also a physician and served humanity. Buddhism not only influenced ayurveda; a practice of medicine but influenced each other aspect of human endeavor during this period. Gutama Buddhatraveled on foot all over north and east part of India preachingnobel way by inspired talks, logical discussions and accepting the ayurveda. Along with Buddhism, Indian traditional ayurveda medicine system flourished in other country like Srilanka, Burma, Bangladesh, Vietnam, and China, Tibet, Island of Sumatra, Taiwan, Myanmar, Thailand; Java ,Cambodia, Japan, Korea. Buddhism promoted ayurveda in the universities of Nalanda andTaxila in 5th century. KingAshoka (disciple of Buddha) established hospital and road side clinics for treatment of ailing patient of poisoning at different part of his kingdom .At Nalanda he established a residential medical institution for teaching and training in toxicology[34].

Kautilya era(6th-7th century) - Kautiya advised medical examination of dead body in a case of unnatural death and suggested board for recording death and birth .He prescribed moral principal for the

physician in there dealing with their patient and this moral principal can be compared with today's medical ethics and code of conduct. It is compulsory for all physicians to register himself or herself in front of king; akin concept of medical registration of those days. Kautilya wrote the book "Arthasasthra" to established justice, foreign policy and implementation of the civil and criminal law. Abortion, infanticide, sexual offence, assault, adulteration, providing false evidence, poisoning, extortion, and injury leading to death, gambling, robbery etc. were punishable with death sentence. False witness being liable to paying ten times the amount lost or gained through the evidence. Kautilya's Arthasastra shows a highly developed technical skill and medical knowledge in criminal justice including rules for judge's appointment. Physician negligence towards patients and state was punishable offence. Prescribing secret and magical remedies were prohibited at the time[35].

Moghul period (15 -16 century) – Moghuls introduced Unani system of medicine in India; there was no expansion of Ayurvedic system of medicine. Crimes were more in this period and punishment was same except cutting of body parts[36].

British East India Company[37,38] (17 century - 1947) -East India Company not only settled in 17thcentury but conquered the India and introduced legal procedure , western system of modern medicine. First recorded medico-legal autopsy in the history of Indian forensic medicine done by British doctor Edward Bulkely on 28 august 1693 on an alleged case of arsenic poisoning. First teaching medical school was establishing in year of 1822 in Kolkata (India) to teach modern medicine. Teaching Ayurveda institutions were established in 1827 and 1916 in Kolkata (India) and Banaras (India) in 1922.Indian penal code come into existence in 1860 and British introduced coroner system in Kolkata and Mumbai by coroner act1871 and Indian evidence act was passed in 1872.Indian medical degree act was passed in 1916 to regulate the grant of titles implying qualification in Western Medical science [39].The false assumption of Western Medical title is punishable offence under this act.

Post-independence

After the independence medical system was divided by two act i.e-Indian medical council act 1956 for controlling Western Medical science and Indian medicine central council act 1970 for regulating Indian Ayurveda Medicine. Indian medicine central council function are maintains a register of medical practitioners, renewal of registration ,

regulation of standard of undergraduate and post graduate Ayurveda education , disciplinary control[40].The drugs and cosmetic rules 1945 and amendment have been framed for regulate the functions and procedures to be followed by central drug laboratory, manufacture control. Under these rules, drugs have been classified under certain schedules for storage, display, prescribing of various drugs and poisons. Schedule "E" of drugs and cosmetic act include poisonous ayurvedic drugs are[41]-

I. *Drugs of vegetable origin :*

- Ahipena -*Papaversomniferum*Linn.
- Arka - *Calotropisgigantea (linn*.)R. Br. ex. Ait.
- Bhallataka-*Semecarpusanacardium*Linn. F
- Bhanga- *Cannabis sativa* Linn.
- Danti -*Baliospermummonatanum*Mull. Arg
- Dhattura- *Datura metal* Linn.
- Gunj- *Abrusprecatirius*Linn.
- Jaipala (Jayapala)- *Croton tiglium*Linn
- Karaveera- *Reriumindicum*Mill
- Langali- *Gloriosasuperba*Linn
- ParasikaYavani-*Hyoseyamusinibar*Linn
- Snuhi*Euphorbia neriifolia*Linn
- Vatsanabha-*AcontiumChasmanthum*StapfexHolm
- Vishamushti-*Strychnoxnuxvomica*Linn.
- Shringivisha-*Acontiumchasmanthum*Stapfex Holm.

II. *Drugs of Animal Origin :*

- SarpaVisha - Snake poison

III. ***Drugs of Mineral Origin :***

- Gauripashana -Arsenic
- Hartala- Arseno sulphide
- Manahashila- Arseno sulphide
- Parada -Mercury
- Rasa Karpura -Hydrargyrisubchloridum
- Tuttha- Copper sulphate
- Hingula- Cinnabar
- Sindura- Red oxide of lead
- Girisindura- Red oxide of mercury

These Schedule "E" drugs which can only be dispensed on the prescription of registered Ayurveda medical practitioners.

The progress of development in Agadatantra has been astonishing in early part of 15th century but it has been remarkable progress after the 1970 to still date by in India. Agadatantra(Indian Forensic medicine and Toxicology) is taught as a part of undergraduate and post-graduate study curriculum by CCIM in all Indian health universities.3 year post-graduate training leading to awards of MD (Ayu) degree in Agadatantra (Forensic medicine and Toxicology) as prescribed by Central Council of Indian Medicine (A

Statutory Body Under IMCC Act 1970, Ministry of AYUSH, Government of India) was first started in Maharashtra (India) at Shri Ayurveda College in 1996[42]. Department of AYUSH; Ministry of Health &Family Welfare and CCRAS give more importance in toxicological pre clinical and clinical study of Ayurveda drug and include it in National Pharmacovigilance Program under Central Drugs Standard Control Organization (CDSCO) in 2004. Every year one representative from subject specialties-Agadatantra, nominated by Department of Ayush will be select for monitoring adverse drug reaction (ADR) of ASU drug[43].

DISCUSSION

Knowledge about the use of metals for weapons, poison and medicine existed amongst the inhabitants of Indus valley civilization. Manusmriti was the documented rule of law in the ancient Indian society and forms the basis of many existing laws. Charaka has given code of ethics for medical practices including charaka shapath which are very similar and relevant to the Hippocratic Oath followed in modern medical sciences. The elaborate classification of visha and the agadayogas (antitoxic formulations) are contributions useful in diagnosis, prognosis and treatments. Sushruta specifically added detailed knowledge about weapons, instruments, fractures, injury, wounds, poisonous damsels, forensic psychiatry etc. apart from the toxicological aspects. Vaghbhat gave continuity to the focus on garavisha and doosivisha and added abundant number of agadayogas for treatment of poisonous cases. Kautilya contributed with laws regarding the medical practices and added to the knowledge regarding the postmortem examination. Development slowed down during the Moghul period and British era. However, after independence, several acts were passed which again brought Ayurveda back to mainstream. Though, the agada practice on toxicological aspects and poisoning cases took back seat, but the acts like Drug and Cosmetic act, establishment of CCIM and Ministry of AYUSH has recognized Agadatantra once again.

CONCLUSION

Agadatantra being a specialized branch of Ayurveda, lots of importance has been given to the related topics in Ayurveda treatises. The legal implications associated with the subject and its scope underwent drastic changes over the years with change in the regimes and rules. However, it has underwent marked evolution with many

acts being passed and laws being framed regarding the medical practices, poisons, drugs and other forensic and medicolegal issues. While the references is in Ayurveda treatise regarding the Forensic and Toxicological aspects is voluminous, the evolution with added information's and changes is appreciable with the time.

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REFERENCES

1. Mukharjee, J.B. (2011). History of Forensic Medicine. In Karmakar, R.N (Ed), *Forensic Medicine and Toxicology* (pp. 1-7). Kolkata: Academic Publishers.
2. Richard, S.U.L.L.I.V.A.N. (1996). The identity and work of the ancient Egyptian surgeon. *JOURNAL OF THE ROYAL SOCIETY OF MEDICINE*, 89(J R Soc Med 1996;89), 467-473.
3. Reddy, K.S.R. (2014). Forensic Medicine. In Murty, O.P (Ed), *The essentials of Forensic Medicine and Toxicology* (pp. 1-5). New Delhi: The Health Sciences Publishers.
4. Mukharjee, J.B. (2011). History of Forensic Medicine. In Karmakar, R.N (Ed), *Forensic Medicine and Toxicology* (pp. 1-7). Kolkata: Academic Publishers.
5. Grover, Nivedita&Tyagi, Isha. (2014). Development of Forensic Science and Criminal Prosecution-India. *International Journal of Scientific and Research Publications*, 4(12), 1-7.
6. Biswas, G. (2015). Inorganic Metabolic Irritants-Arsenic. In Paul, G (Ed), *Review of Forensic Medicine and Toxicology* (pp. 489-493). New Delhi: The Health SciencesPublishers.
7. Wikipediaorg. (2018). *Wikipediaorg*. Retrieved 23March,2018, from https://en.wikipedia.org/wiki/Felice_Fontana
8. Grover, Nivedita&Tyagi, Isha. (2014). Development of Forensic Science and Criminal Prosecution-India. *International Journal of Scientific and Research Publications*, 4(12), 1-7.
9. Biswas, G. (2015). Inebriants-Alcohol. In Paul, G (Ed), *Review of Forensic Medicine and Toxicology* (pp. 542-575). New Delhi: The Health SciencesPublishers.
10. Ccimindiaorg. (2018). *Ccimindiaorg*. Retrieved 23March,2018, from https://www.ccimindia.org/
11. Pillay,V.V. (2013). Irritant Plants. In Prem,N (Ed), *Modern MedicalToxicology* (pp. 117-131). New Delhi: JAYPEE.
12. Schug, G. R., Gray, K., Mushrif-Tripathy, V., &Sankhyan, A. R. (2012). A peaceful realm? Trauma and social differentiation at Harappa. *International Journal of Paleopathology*, *2*(2-3), 136-147.
13. Schug, G. R., Gray, K., Mushrif-Tripathy, V., &Sankhyan, A. R. (2012). A peaceful realm? Trauma and social differentiation at Harappa. *International*

Journal of Paleopathology, *2*(2-3), 136-147.

14. Gwen, R & Mushrif Tripathy, V. (2009). Ancient Skeletal Evidence for Leprosy in India (2000 BC). *PLOS ONE*, 4(5), 1-8.

15. Mukharjee, J.B. (2011). History of Forensic Medicine. In Karmakar, R.N (Ed), *Forensic Medicine and Toxicology* (pp. 1-7). Kolkata: Academic Publishers.

16. Wasedarvishwanath, S & kapoor, T.E.E.N.A. (2017). Chronic Liver Disease Management Garavisha (Artificial Poison)–A Case Report. *IAMJ*, 1 (3) (ISSN: 2320 5091), 364-368.

17. Drdhabala. (2011). Madataya. In Sharma, P.V. (Ed), *Charak Samhita* (pp. 390-417). Varanasi: Chaukhambha Orientalia.

18. Ballav et al. (2017). VISHAJA VRANA: A LITERARY REVIEW. *Int J Res Ayurveda Pharm*, 8 (Suppl1), 22-24.

19. Sunitha et al. (2017). CHATHURVIMSHATHI UPAKRAMA AND ITS IMPORTANCE: A REVIEW. *Journal of Biological & Scientific Opinion*, 5(1), 6-10.

20. Namburi, U.R. (2010). Introduction to visha. In S (Ed), *The Text Book of Agatatantra* (pp. 7-17). New Delhi: Chaukhambha Publications.

21. Dalhana. (2010). Kalpasthan. In Sharma, P.V. (Ed), *Susrutasamhita* (pp. 3-102). Varanasi: Chaukhambha Visvabharati.

22. Dalhana. (2010). Kalpasthan. In Sharma, P.V. (Ed), *Susrutasamhita* (pp. 5-100). Varanasi: Chaukhambha Visvabharati.

23. Nitin, U. (2010). Sarpa. *The Text Book of Agatatantra* (pp. 133-157). New Delhi: ChaukhambhaOrientalia.

24. Pillay,V.V. (2013). Venomous Bites and Stings. In Prem,N (Ed), *Modern MedicalToxicology* (pp. 139-140). New Delhi: JAYPEE.

25. Nitin, U. (2010). Sarpa. *The Text Book of Agatatantra* (pp. 135-136). New Delhi: ChaukhambhaOrientalia.

26. Pillay,V.V. (2013). Venomous Bites and Stings. In Prem,N (Ed), *Modern MedicalToxicology* (pp. 140-141). New Delhi: JAYPEE.

27. Nitin, U. (2010). Sarpa. *The Text Book of Agatatantra* (pp. 135-136). New Delhi: ChaukhambhaOrientalia.

28. Pillay,V.V. (2013). Venomous Bites and Stings. In Prem,N (Ed), *Modern MedicalToxicology* (pp. 140-141). New Delhi: JAYPEE.

29. Usturage, R.R, Pawade, U.V &Supugade, V. (2015). CRITICAL REVIEW OF COSMETIC TOXICITY WSR DUSHI VISHA. *International*

Ayurvedic Medical Journal, 3(15), 2539-2546.

30. Sourav et al.. (2017). VISHAJA VRANA: A LITERARY REVIEW. *Int J Res Ayurveda Pharm*, 8(Suppl1), 22-24.

31. Aravind et al.. (2017). CONCEPTUAL STUDY ON ANTI-TOXIC ACTION OF KSHARA AGADA: A REVIEW. *Int J Res Ayurveda Pharm*, 8(1), 19-21.

32. Dalhana. (2010). Kalpasthan(Chapter 3). In Sharma, P.V (Ed), *Susrutasamhita* (pp. 27-31). Varanasi: ChaukhambhaVisvabharati.

33. Vagbhat. (1997). Uttarasthana. In Murthy,K.R.S (Ed), *AstangaHrdayam* (pp. 329-378). Varanasi: Krishanadas Academy.

34. Pandey et al.. (2015). IMPORTANCE OF BUDDHISM IN AYURVEDA. *WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES*, 4(5), 466-473.

35. Kangle, R.P. (2010). Arthasastra part 3. In K, R.P (Ed), *TheKautilyaArthasastra* (pp. 1-297). Delhi: Motilalbanarsidass publisher PVT LTD.

36. Mukharjee, J.B. (2011). History of Forensic Medicine. In Karmakar, R.N (Ed), *Forensic Medicine and Toxicology* (pp. 1-7). Kolkata: Academic Publishers.

37. Mukharjee, J.B. (2011). History of Forensic Medicine. In Karmakar, R.N (Ed), *Forensic Medicine and Toxicology* (pp. 1-7). Kolkata: Academic Publishers.

38. Mittal, S. (2007). Evolution of Forensic medicine in India. *JIAFM*, 29(4), 89-91.

39. Biswas, G. (2015).Medical Jurisprudence and Ethics. In Biswas, G (Ed), *Review of Forensic Medicine and Toxicology* (pp. 489-493). New Delhi: The Health SciencesPublishers.

40. Ayushgovin. (2018). *Ayushgovin*. Retrieved 23March,2018, from http://ayush.gov.in/sites/default/files/The Indian Medicine Central Council Act, 1970.pdf

41. Whoint. (2018). *Whoint*. Retrieved 23 March,2018, from http://apps.who.int/medicinedocs/documents/s20107en/s20107en.pdf

42. Joglekar, V.P. (2008). Introduction to Agadatantra. In Huparikar, S.G &Joglekar, V.P(Eds), *The Text Book of Agatatantra* (pp. 3-6). Pune: Rashtriya Sikshan Mandal.

43. Whoint. (2018). *Whoint*. Retrieved 24March, 2018, from http://apps.who.int/medicinedocs/documents/s17085e/s17085e.pdf