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Review Article

ARSENICALS REVIEW: POISON VIS-A-VIS MEDICINE

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ABSTRACT

Arsenic tops the list of priority list of hazardous substances 2022. People are frequently exposed to the environmental pollutant metalloid arsenic through their food, water, air, and soil. Arsenic is famous for its toxic effects. However, arsenicals have recently gained attention due to promising clinical trials for the treatment of acute myeloid leukemia. Presently numerous studies on arsenic's anticancer effects have been done. So a review was conducted on the use of arsenicals as poison and medicine. Arsenical was used as a powerful medicine in the BC era. But arsenical became famous as "the King's Poison" and "the Poison of the King" due to its use as poison. But the development of Marsh's Test in the 18th century led to a decrease in the use of arsenicals as poison. In the 18th century, arsenicals were used as medicine to treat a variety of diseases such as fever, rheumatism, psoriasis, and syphilis. The development of antibiotics, new, safer chemotherapeutic agents, and radiotherapy halted its use as medicine. The dose and form of arsenicals make them medicine or poison. Many literary works reveal that arsenic's journey as "medicine" and "poison" is still ongoing in the twenty-first century.

INTRODUCTION

A recent poisoning death of a Mumbai businessman [1] and a Carmelo Gurnari et al. article on "When Poisons Cure"[2] have highlighted the use of arsenicals as both a poison and a medicine. Arsenic, a ubiquitous substance, is prevalent in our environment and a natural environmental pollutant to which humans are constantly exposed through food, water, air, and soil. The most recent Comprehensive, Environmental, Response, Compensation, and Liability Act (CERCLA) Priority List of Hazardous Substances issued by the Agency for Toxic Substances and Disease Registry (ATSDR, 2022) places arsenic at the top of the list. [3] Many studies are being conducted on the use of arsenicals in cancer treatment.[4] Arsenic has been used as medicine and poison since antiquity. Here an attempt is made to contemplate the journey of arsenicals as medicine-poison-medicine-poison.

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Arsenic as Medicine in the BC Era

Since ancient times, the Greek and Roman civilizations have used arsenic compounds like orpiment and realgar as medicines.[5] It is believed that Hippocrates used an arsenic paste to treat abscesses and ulcers. [6] Dioscorides was a Greek herbalist and surgeon who served in Nero's army. He made detailed studies on asthma, including the use of realgar combined with resin, smoked as a smoke for the treatment of cough, or administered as a potion for asthma.[5] Arsenic sulphide was advised as a treatment for ulcers by the Greek physician Galen (129–210 AD). [6]

Arsenicals in Chinese Traditional Medicine

The Chinese traditional medicines make use of orpiment (*Cihuang*), realgar (*Xionghuang*), and arsenolite (*Pishi*). Examples of the three main minerals containing arsenic used in Chinese traditional remedies are shown in Table 1.[7] The first book on Chinese traditional medicine, Shen Nong Ben Cao Jing, was compiled during the Eastern Han dynasty, and it agrees with the Chinese Nei Jing Treaty (263 BC), which described the usage of arsenic pills for the treatment of periodic fever. Malaria was treated using a mixture of realgar, orpiment, and ATO by Sun Si-Miao (581-682 AD), a Chinese physician known as China's King of Medicine.[8] In traditional Chinese medicine, the

idea of using one toxin to combat another or to combat cancer is quite widespread.[9,10] Today, orpiment, realgar, or arsenolite are still used in hundreds of traditional Chinese medicines, and realgar alone is present in 22 oral cures according to the Pharmacopeia of China (2005). [10]

Table 1: Examples of Orpiment, Realgar and Arsenolite/Arsenic trioxide in Traditional Chinese Medicines

Arsenicals	Traditional Medicines	Recipe	Therapeutic effects
Orpiment[7,10]	Used alone	External use	Scabies, louse-killer, snake biting, skin diseases
	Quingyu Piwen Dan	One of 74 herbs	Detoxication, diarrhea, abdominal pain
Realgar [7,10]	*Niuhuang Jiedu Pian*	6.4% realgar in 8 herbs	Antipyretic, common cold, gingivitis, toothache
	Shuzheng Pian	7.1% realgar in 15 herbs	Heatstroke, dizzy, coma, diarrhea
	Hongling San	15% realgar in 7 Components	Heatstroke, dizzy, headache, nausea
	Xiao'er Huadu San	11.5% realgar in 7 components	Children detoxication for fester, malignant boil
	Liushen Wan	one of 6 components	Tonsillitis, laryngitis, throat pain, common cold
	Yatong Yili Wan	10% realgar in 4 herbs/minerals	Toothache, gingivitis, dental caries
	Angong Niuguang Wan	10% realgar in 11 herbs/ minerals	Coma, unconscious, delirium, convulsions
	jujabg Zhwao San	12% realgar in 9 herbs/ minerals	Fever convulsions, delirium, coma
	Shayao	11 % realgar in 11 herbs/ minerals	Heat stroke, coma, abdominal pain
	Xiao'er Qizhen Wan	15% realgar in 19 herbs/ mineral	Children sedatives, antipyretic, laxative
	Jinhuang Baolong Wan	10% realgar in 6 herbs/ minerals	Phlegmesia, asthma, antispasmodics
	Awei Huapi Gao	4% realgar in 24 components	Remove lump and pain, malignancies
Arsenolite[7,10]	Used alone	External or internal use	Remove lump, scrofula, scabies, anti-parasites
	Ailing Yihao	Major component of the mixture	Leukemia and malignancies

All the recipe and uses are based on Pharmacopeia of China (2005)

Ayurvedic (Indian System of Medicine) Arsenicals

According to Ayurveda, everything on earth is a medication, but the dosage and method of use determine whether it is a medicine or a poison. The characteristics of the nectar can also be improved by the use of poison in little amounts, according to ancient experts.[11] Arsenical was used by Ayurveda under the names *Hartala* (Orpiment), *Manshilla* (Realgar), and *Somal* (Arsnolite). [12] (See figure 1) The negative effects or poisonous nature of these arsenicals are well known to *Ayuvedacharya*.[13,14,15] They created some unique processes, such as *Shodhana* and *Marana*, to transform these lethal chemicals into powerful medications. Both internally (orally) and externally (in the form of ointment or medicinal vapours), these arsenicals are employed. Table 2 elaborates on the specifics of these arsenicals' medicinal efficacy according to Ayurveda. The various formulas listed in the Ayurvedic pharmacopoeia continue to use a variety of formulations that contain orpiment, realgar, and arsenolite.

Table 2: Arsenicals as a Medicine in Ayurveda

S.No.	Name of the Arsenicals	Route of Administration	Dose	Therapeutic Effects
01	*Hartala* (Orpiment)	Oral and external	¼ to ½ *Ratti*[16] 30-60mg per day in divided doses.	*Kushta* (skin diseases), *Vata vyadhi* (diseases of *vata*), *Agnimandya* (indigestion), *Shula* (abdominal pain), *Gulma* (tumour), *Pleeharoga* (disease of spleen), *Kasa* (cough), *Swasa* (asthma), *Kshaya* (emaciation), *Nadi Vrana* (sinus ulcers), *Bhagandara* (fistula), *Vatarakta* (arthritis), *Phiranga* (syphilis).[17]
02	*Manashilla* (Realgar)	Oral and external	1/32 to1/16 *Ratti*[18] 3.75-7.5mg per day in divided doses.	*Kasa* (cough), *Swasa* (asthma), *Kshaya* (emaciation), *Agnimandya* (indigestion), *Anaha* (flatulence), *Kandu* (puritis), *Jwar* (fever), *Vishapaha* (antidote to poisons) [19]
03	*Somal* (Arsenolite)	Oral and external	1/120 to 1/30 *Ratti* [20] 1-4 mg per day in divided doses.	*Swasa* (asthma), *Kushta* (skin diseases), *Sandhigata Vata* (joint disorders) *Phiranga* (syphilis), *Agnimandya* (indigestion), *Visham Jwar* (intermittent fever), *Jeerna Pandu* (chronic anemia), *Jwarotha Hrudya Daurbalya* (fever induced myocardial weakness), *Atisara* (diarrhoea), *Vruchhika Danshahar* (local application in scorpion bite), *Shotha* (odema) [21]

Arsenic as "King's Poison"

During the middle ages and the renaissance, ancient emperors employed arsenicals with the aim of eliminating members of the ruling elite. [22] To ensure his position on the Roman throne, the fifth emperor Nero ordered the poisoning of his 13-year-old stepbrother Britannicus. [23] Pope Alexander VI (1431–1503), a member of the Borgia family, one of the most illustrious families of the Italian Renaissance, murdered cardinals for their possessions using the notorious powder known as “cantarella”, which is usually thought to have contained primarily arsenic.[24] According to some conspiracy theorists, Napoleon Bonaparte's assassination in 1851 was motivated by politics. [25]

Arsenic as "Poison of the King"

Prior to the Marsh Test's creation in the middle of the 18th century, arsenic was the most popular homicidal and suicidal poison used by individuals. Inorganic arsenic compounds, such as arsenic trioxide (white arsenic), are tasteless and odourless, making them perfect poisons. Heating arsenic ore generated a white, crystalline powder that was easily produced and almost undetectable in food and drink. Some people even claimed it enhanced the flavour of wine. [26] Two murder trials occurred in the middle of the 19th century, one in France and one in Edinburgh. Madeleine Smith, a socialite from Glasgow, was charged with killing her lover with a drink of cocoa that had been poisoned with tasteless, colourless arsenic. The verdict was "not proven," which is unique to Scots law.[27] In 1839, Marie Lafarge was accused of killing someone with arsenic.[28] The "Affair of the Poisons" in the French court of Louis XIV, where Catherine Deshayes gave ladies the arsenic-based poison "La Poudre de Succession" or "inheritance powder" to help them get rid of their husbands, is a well-known case of arsenic poisoning. [29] Toffana and her daughter Girolama were the creators of the arsenic-filled Aqua Toffana cosmetics. In 1659, both were put to death in Rome for their involvement in the poisoning deaths of many hundreds of individuals. [30]

Major Developments Related to Arsenicals

It is well known that the father of toxicology and pharmacology, Paracelsus (1493–1541 AD), a Swiss physician, utilized elemental arsenic frequently.[24] The Marsh Test, which was developed in 1836 to identify arsenic poisoning, is a significant turning point in the history of arsenic. This test was created by English chemist James Marsh and further improved by Swedish scientist Jöns Jacob Berzelius. Following the Marsh Test, arsenic poisoning cases substantially decreased. [31,32]

An effort was made to address this with the Arsenic Act of 1851. Arsenic was only available to people who were at least 21 years old. It needed to be blended with indigo or soot. A register that was fully filled out with the buyer's name, address, and intended usage had to be signed by both the buyer and a third

party witness. The buyer had to be known to the supplier unless the arsenic was ordered by prescription. The Poisons Act of 1868 made improvements to the shortcomings of the earlier Act, but it wasn't until 1933 that the Poisons and Pharmacy Act made it necessary to list the ingredients of any medication on the label.[5]

Arsenicals have been classified as Schedule E-1 of the Indian Drug and Cosmetic Act 1945 since 1970. As per pre-rule 161.2 of the Drug and Cosmetic Act of 1945, the container of a medicine for internal use made up and ready for the treatment of human ailments shall, if it is made up of a substance specified in Schedule E (1), be labelled conspicuously with the words 'Caution: to be taken under medical supervision' both English and Hindi languages. [33]

Arsenicals as Chemical Warfare

Lewisite and Adamsite were created in 1918 by the US Army Chemical Warfare Service to combat the Central Powers' efficient use of gas agents against the Allies in the Western European trenches. The synthesis of the substance and its capacity to be deployed as a gas warfare weapon were both perfected in 1918 by Winford Lee Lewis, a soldier and chemist in the US Army Chemical Warfare Service. The primary function of lewisite is as a vesicant (or blistering agent), but it can also be absorbed and cause systemic poisoning in addition to being a serious respiratory and eye irritant. [32]

Roger Adams, a chemist with the US Army Chemical Warfare Service, created the chemical warfare agent "a adamsite", which is C12H9AsClN, diphenylaminechloroarsine, in 1918. Later in World War II, it underwent testing on the western front. They were not used, however, because it was discovered that they were less effective than other agents at delivering vesicant and respiratory irritating gases.[32]

Arsenicals in 18th-Century Medicine

The queen's physician in Scotland, James Begbie (1798–1869), recommended using arsenic for psoriasis, epilepsy "and various episodes," chronic rheumatism, and chorea (which "required steadily increasing doses").[34] A British physician named Thomas Fowler published his research on 1% potassium arsenite, also known as "Liquor mineralis," in 1786 for "agues, remittent fevers, and monthly headaches." To cure ague (malaria) and "sleeping sickness," the London Pharmacopeia recognised the drug "Liquor Mineralis" in 1809. (trypanosomiasis). Fowler's Solution was prescribed for a number of additional conditions up to the 1880s, including asthma, eczema, psoriasis, anaemia, hypertension, gastric ulcers, heartburn, rheumatism, and TB. [32]

Arsenicals in Medicine in the Nineteenth Century

The use of parsanilic acid as "Atoxyl" to treat human trypanosomiasis by Harold Thomas from Canada and Anton Brenil from Australia in 1905 was terminated due to the drug's neurotoxicity. Arsenophenylglycine, sometimes known as "418," was created in 1907 by Ehrlich and Bertheim and is effective against trypanosomiasis. Later, to cure sleeping sickness, p-glycineaminophenyl arsenate, also known as "Tryparsamide," and melaminophenyl arsenicals, also known as "Melarsen Oxide," were produced. [34]

Paul Ehrlich received the Nobel Prize in 1908 for his work on immunity, serum, and the creation of the first syphilis medication, an arsenical he coined "compound 606" (arsphenamine), later refined into neo-arsphenamine. Ehrlich also originated words like "chemotherapy," magic bullet," and "blood-brain barrier." [35] The American Medical Association's 1914 Handbook of Useful Drugs recognised salvarsan and neo-salvarsan as effective treatments for primary syphilis and spirillar illnesses like relapsing fever and Vincent's angina, as well as for later stages of syphilis when combined with mercury.[36] Arsenicals, namely arsphenamine, neoarsphenamine, acetarsone, and mapharside, in combination with bismuth or mercury, remained the basis of syphilis treatment until the introduction of penicillin in 1943. [37,38]

Arsenical Accidental Poisoning

In the 1900s, drinking beer brewed with arsenic-contaminated components led to an outbreak of arsenic poisoning in England.[39] Arsenic-tainted powdered milk in the 1950s poisoned Japanese newborns. [39] In the west of Scotland, where many youngsters were found to have minor arsenic poisoning symptoms, Scheel's Green was used to colour candies until it was removed off the shelves. Some of these symptoms may have been caused by the blancmange, which was also coloured with Scheel's Green.[5] Arsenic was linked to a dramatic mass poisoning in Japan in 1998 that resulted in four fatalities and 40 hospitalizations. Pots of curried meat had been laced with arsenic trioxide and served during a local festival.[40] In 1943, 150 students and two members of the public fell ill with arsenic poisoning, which was linked to locally manufactured sausages and brought unwanted attention to a college affiliated with St. Andrews University. [26]

There are several areas where drinking water is significantly contaminated by arsenic, and arsenic contamination of groundwater is ubiquitous. Arsenic levels in the water that an estimated 140 million people have been consuming have exceeded the WHO interim guideline value of 10g/L in at least 70 different nations. This is in line with current statistical modelling, which indicates that 94 to 220 million

individuals may be at risk of exposure to groundwater with elevated arsenic contents.[41]

Arsenic Eaters[5,29]

The myth of the arsenic-eaters of Syria, a hilly area in southeast Austria, fueled interest in the nineteenth century. While the males reported that eating arsenic scraped from the rocks enhanced their breathing on hard mountain climbs, the Syrian women stated that consuming arsenical compounds helped their complexion and made them more desirable to the men. Dr.Robert Craig MacLagan of Edinburgh travelled to the Styrian village of Liegist, where he talked with some local physicians who confirmed the practice and observed two individuals using arsenic, also known as Hydrach or Hutterricht. He was informed that the majority of the local men consumed it twice per week, felt deficient in it otherwise, and took an average of 6 grains per dose. He observed men spreading it on bread and consuming it with water, just like those who followed him.

Arsenicals as a Ray of Hope in Cancer

In traditional Chinese medicine, the idea of using one toxin to combat another or to fight cancer is a popular one.[9,10] Fowler's solution was first used to treat chronic myelogenous leukaemia in 1878, and until the development of radiation therapy and chemotherapy in the 20th century, it was the predominant leukemia treatment.[42] The 1914 edition of the American Medical Association's Handbook of Useful Drugs listed sodium arsenate and arsenic trioxide as treatments for protozoal illnesses, syphilis, malaria, and chronic inflammatory skin conditions. [36]

Sulphydryl inhibitors, which included oxophenarsine, were created in the 1960s but were supplanted by other anticancer medications a decade later. Arsenic trioxide was helpful in treating acute promyelocytic leukaemia (APL) both when it first developed and when it relapsed, according to multiple Chinese studies conducted in the 1990s (APL). Arsenic trioxide was licenced by the US FDA in 2000 for the treatment of APL.[42,43] Researchers at the University of Arkansas for Medical Sciences discovered in 2001 that arsenic trioxide can successfully treat advanced, high-risk multiple myeloma. [44] There are numerous studies being done on the use of arsenic in various cancer treatments. Akinobu Ota et al. mentioned in their article that arsenical compounds enhance cancer cell apoptosis when combined with other anticancer therapeutics, including radiation, chemotherapies, and molecularly targeted drugs. [4]

Table 3: Timeline: Arsenicals as Medicine

Period	Arsenic Compound	Product Name	Nation and Scientist Details	Disease or other Remark
370 BC	Arsenic tri and disulphide	Orpiment, Realgar	Greek Hippocrates	Abscess, ulcer, skin cancer[6]
	Arsenic Trisulphide	Orpiment	Discorides	Depilatory[5]
384-322	Realgar	Sandarche	Arsitotle[7]	
263 BC		Arsenic Pills	Chinese traditional medicine	Periodic fever[7]
23-79 AD	Arsenic Trisulphide	Auripigment	Piny the Elder[45]	
129-210 AD	Arsenic Sulphide		Greek , Galen	Ulcers[8]
581-682 AD	A Combination of Arsenic Sulphide and Oxides		Chinese Sun Si- Miao	Malaria[8]
980-1037	Arsenic trioxide	Arsenolite	Persian Avicenna	Fevers[8]
1493-1541	Elemental As	-----	Swiss Paracelsus	Invention of elemental as and use of other metals as medicine[8]
1518-93	Arsenic Trioxode	Arsenolite	Shin Zhen Li	Compendium of materia medica for various diseases
1786-1801	1 % K Arsenite	Liquor Mineralis	British Fowler	Malaria, remittent fever, periodic headache[32]
	As tri-iodide and Hg Tri-iodide	Donavans solution	Thomas[32]	

	As Trichloride	De Valagins Solution	Thomas[32]	
18th		Tasteless Ague Drop Asiatic Pills Patent Ague Drops	Pharmacopoeia of Stafford Hospital England	Agues and intermitting fevers[5]
1809	1 % K Arsenite	Fowlers Solution	London Pharmacopiea	Asthma, chorea, eczema, psoriasis, rheumatism, T.B., syphilis and ulcers[32]
1878	1 % K Arsenite	Fowlers Solution		Lowers the blood count in the normal individuals[32]
1880	1 % K Arsenite	Fowlers Solution		Skin and breast cancers[32]
1905	P Arsanilic acid	Atoxyl	Cananda Harold Thomas Australia Anton Breni	Human trypanosomiasis[34]
1907	Arsenophenyl glycine Spilasyl	418	Ehrlich and Bertheim	Trypanosomiasis[34]
		Stovarsol Na acetasone	May and Baker	Tuberculosis[34]
1910	Arsphenamine	606	German Nobel Laureate Paul Ehrlich	Syphilis Spirochates[35]
1912	Arsphenamine	Salvarsan (Silver Magic Bullet)		Syphilis modern era of Chemotherapy[35]
	Neoarsphenamine	914 NeoSalvarsan		Syphilis[35]
1914	Arsenic Trioxide Na Arsenate	Arsenolite	American Medical Association handbook of Useful Drugs	Skin cancer, chronic inflammatory skin disease, malaria, syphilis, protozoal diseases[36]
1919	p glycineamino phenyl arsenate	Tryparsamide	Walter A Jacobs	Trypanosomiasis[34]
1930	Oxo phenarsine HCL	Mapharsen[32]		
1931	Arsenic Trioxide	Arsenolite	Boston city Hospital	Chronic myeloid Leukemia[43]
1940	Melaminophenyl arsenicals	Melarsen Oxide	Ernst A H Fridheim	Trypanosomiasis[34]
1949	Melarsoprol		Ernst A H Fridheim	Gambian sleeping sickness[46]
1970	Arsenic Trioxide	Arsenolite		Acute APL[42-43]
1994-96	Arsenic Trioxide	Arsenolite		Clinical Trials on APL[42-43]
2003	Arsenic Trioxide	Trisenate	US FDA approved	APL[42-43]

Table 4: Timeline: Arsenicals as Poison

Period	Compound Name	Empire/ Nation	Remark
55AD		Rome	Roman Emperor Nero- Arsenic poisoning of 13 yrs old step brother Britannicus[23]
370 BC		Hippocrates	Abdominal colic in miners of metal[32]
4 BC			Theophrashes of Erebus[32]
1431-1503	Cantarella	Italy	Pope Alexander VI – Borgia family to kill cardinals[24]
16-19th	La poudre de Secession Or Inheritance powder	French	Affair of poisons : Woman uses to get rid of their husbands and become young rich widows[29]
1659		Italy	Guilai Toffane and his daughter Giroloma used as tainted cosmetics[30]
1839			Marie Lafarge was tried for murder using arsenic[28]
1851			Napolean Bonaparte political assassinations[25]
1856			Rodolphe lover of Madam Bovary killed by arsenic[5]
1900		England	Poisoning after consumption of beer brewed with As containing ingredients[39]
1911		China	Emperor of China, Guangxu, died as a result of arsenic poisoning[5]
1918	Lewisite Adamsite	United States	Primary Vesicant, potent respiratory and eye irritant developed as chemical warfare[32]
1939			Kesselring aroused further public interest with his play arsenic and old lace in which Martha Brewster used her homemade elderberry wine, 1 gallon of which contained one teaspoonful of arsenic, a half teaspoonful of strychnine and a pinch of cyanide, prompting her nephew Mortimer to remark 'should have quite a kick! [5]
1950		Japan	Infant poisoning through as contaminated powdered milk. [39]
1979			International Agency for Research on cancer – Arsenic as Carcinogenic[47]
20th		Philadelphia and California	13 convictions of women poisoning their husbands for insurance money Philadelphia[5]

Figure 1: *Hartala* (orpiment) *Manshill* (Realgar) *Somal* (Arsenolite)

DISCUSSION

Arsenical ore or derivatives were used as paint pigments before the discovery of elemental arsenic. Arsenicals have been used as medicine since the BC era, as is seen from literature about the Greek, Chinese, and Indian emperors. Arsenics later became known as the "King of the Poison" and "Poison of King's." Arsenic was a popular poison from the 16th to 18th centuries because it is a colorless, odourless powder that dissolves easily in water and is undetectable with the tools available at the time. The Marsh test, developed in 1836, aided in the detection of arsenic in hair and nails. The invention of the Marsh test stalled the use of arsenic as a poison.

Meanwhile, Chinese traditional medicine uses arsenic as a treatment based on the idea that one poison can neutralize another. The Indian System also emphasizes that every material has a purpose based on how it is used and in what quantity. Ayurveda also advises using poison in conjunction with nectar to improve the nectar's characteristics. Everything contains poison, and nothing is free from it. It can be a poison or a cure, depending on the dose.[48] Arsenic was one of the minerals and compounds that Paracelsus supported for use in medicine, stressing that the amount determines whether a substance is a drug or a poison. These quotations are most appropriate for arsenic and arsenicals. Arsenic was used as medicine to treat different conditions like intermittent fever, rheumatism, syphilis, and sleeping sickness in the 18th and mid-19th centuries. The development of penicillin like antibiotics, radiotherapy, and new chemotherapeutic agents, as well as the toxicity caused by arsenical medicines has led to the decline of arsenical as a medicine. But recent research on arsenic in the treatment of leukemia has brought the use of arsenicals to light to treat many cancers. Arsenic's toxicity is the main barrier to its usage as medication. Therefore, it is necessary to employ recent scientific advancements and collaborate with ancient medical systems like Ayurveda and Chinese medicine to create next generation arsenicals that can overcome the drawbacks of currently employed arsenic-based medications.

CONCLUSION

Arsenic is one of the most toxic elements on Earth. Many people are exposed to arsenic through drinking water, which leads to toxic changes. A thorough examination of arsenicals reveals that they have been used as potent medicine since the BC era. Arsenicals were the most famous poisonous substance until the development of Marsh's test in the mid-18th century. Arsenicals were used as powerful medicine in the 18th and 19th centuries. In the nineteenth century, the development of antibiotics and new, safer chemotherapeutic agents reduced the use of arsenicals. Recently, arsenical has been in the spotlight once again due to its effective action on acute promyelocytic leukaemia (APL). Arsenicals are both poison and potent medicine due to their dosage and forms. To summarize, arsenic has a long history as both a medicine and a poison that continues to this day.

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