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REVIEW

Arsenic in Drinking Water: A Review on Toxicological Effects, Mechanism of Accumulation and Remediation

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The aim of this review article is to bring out the toxicological effects caused by arsenic on the biological systems. Drinking water is the major direct source of arsenic exposure by general population. The two predominant species of arsenic are arsenate [As(V)] and arsenite [As(III)]. Arsenite is much more toxic. The review covers a bibliometric analysis of drinking water from 1991 to 2008 covering 2,299 publications on the subject. The data source and case study section highlights the historical and present evidences of arsenic toxicity. The effect of toxicity, biomarkers of arsenic toxicity and the mechanism of arsenic toxicity on plants and animals and sources of remediation are well reported in the article. Lastly various treatment technologies to minimize or remove arsenic are reported.

Key Words: Arsenic, Drinking water, Bibliometric analysis.

INTRODUCTION

Arsenic is a ubiquitous element that ranks 20th in abundance in the earth's crust, 14th in the seawater and 12th in the human body[1]. It comprises about five hundred-thousandths of 1 % (0.00005 %) of the earth's crust[2]. It is widely distributed in nature in the form of either metalloids or chemical compounds, primarily present in inorganic forms and exists in two predominant species: arsenate and arsenite. Arsenite is much more toxic[3], soluble and mobile[4] than As(V). Arsenate (as $H_2AsO_4^-$ and $HAsO_4^{2-}$) is the predominant form of arsenic in well-oxidized waters, while arsenite occurs predominantly as $H_3AsO_3^0$ and $H_2AsO_3^-$ in reduced environments[5].

Albertus Magnus in 1250 AD for the first documented the hazardous effects of arsenic[6]. Since then arsenic has been a center of controversy in human history. Arsenic is well known for its hazardous effects on both flora and fauna. The consumption of arsenic contaminated water is the main path for its transportation into the environment and biological systems[7-13]. The use of arsenical drugs in the production of food animal is an anthropogenic source of arsenic exposure. These drugs results in residual contamination of animal food products, as well as environmental contamination associated with disposal of wastes from these animals. The land disposal of these wastes can contaminate surface and ground water indirectly[14].

It has been known for many years that arsenic is soon fatal when ingested at high doses, the effects of low dosages became apparent in the 1980s[15]. The World Health Organization (WHO) guideline value for arsenic in drinking water is 10 µg/L[16]. In Japan, the permissible limit of arsenic in drinking water is 10 µg/L[17]. The United States maximum contaminant level for arsenic in drinking water was set at 50 µg/L (old limit)[18]. While, the new maximum contaminant limit for arsenic in drinking water in United States is 10 µg/L[19]. In Canada the old limit was 25 µg/L[18] which is lowered to 10 µg/L in 2006.

Arsenic is commercially used as pesticide. It is also used in the manufacture of glass, paper and semiconductors. Most of the arsenic derived pesticides, such as lead arsenate, Ca_3AsO_4, copper acetoarsenite (Paris-Green), H_3AsO_4, monosodium methane arsonate (MSMA), disodium methane arsonate (DSMA) and cacodylic acid are used in cotton production[20]. The inorganic arsenicals, primarily, sodium arsenite, were widely used since 1890 as weed killers, particularly as non-selective soil sterilants[21]. Arsenic acid used extensively as a cotton desiccant for many years. Two thousand and five hundred tons of H_3AsO_4 was used as desiccants on

1,222,000 acres (*ca.* 495,000 ha) of U.S. cotton in 1964[22]. Fluor-chrome-arsenic-phenol (FCAP), which was used as early in 1918 in USA as a wood preservative contains arsenic. Arsenic and its compounds are infamous as very potent poisons and are preferred to homicidal and suicidal agents. Even the death of Napoleon Bonaparte was suspected to be due to As poisoning[23]. This review covered the effect of arsenic toxicity on animals and human beings. The mechanism of arsenic accumulation in plants and animals along with the biomarkers of arsenic toxicity and the sources of remediation were covered. The bibliometric analysis was done to report the current concern regarding the topic.

Bibliometric analysis of drinking water publication: The data were based on the online version of the Science Citation Index-Expanded (SCI-Expanded), Web of Science. SCI-Expanded is multidisciplinary database of the Institute for Scientific Information (ISI), Philadelphia, USA. According to Journal Citation Reports (JCR), it indexes 6,426 major journals with citation references across 172 scientific disciplines in 2007. The online version of SCI-Expanded was searched under the keywords ("drinking water," "drinking waters," "drinkable water," "drinkable waters," and "drinking waterborne") and ("arsenic," "arsenate," and "arsenite") as a part of title, abstract, author keywords and keywords plus to compile a bibliography of all papers related on arsenic in drinking water research.

The total number of publications that met the selection criteria was 2,299. These publications were divided into 12 document types. The most frequently used document type were articles (1,809; 79 %), followed distantly by proceedings papers (183; 8.0 %) and reviews (141; 6.1 %). Other document types of less significance were meeting abstracts (85; 3.7 %), editorial materials (39; 1.7 %), letter (18; 0.78 %), news items (18; 0.78 %), corrections (2; 0.087 %) and one for discussion, reprint, addition correction and note, respectively. Since peer reviewed journal articles represents the majority of documents within this field, 1,809 articles were further analyzed.

Fig. 1 shows the article output results from 1991 to 2008. The number of articles per year increased from 8 in 1991 to 292 in 2007 and 269 in 2008, reflecting the increasing interest in this topic of research. Fifty-five percent of the records were published during the period 2005 to 2008. In total, 1,908 articles were published in 441 journals. Table-1 presents the 14 core journals contained 34 % of the total articles. Environmental Health Perspectives ranked first with 94 (5.2 %) published papers followed by Environmental Science & Technology with 74 (4.1 %) publications. According to the results of analysis in subject category, nine core journals belong to environmental sciences, followed by environmental engineering with five journals and water resources with four journals. Fig. 2 shows the trend of article publication in six most productive journals from 1991-2008. It reflects that in between 1991 to 2001 the number of articles published per year is below ten. In this period (1991 to 2001) the maximum numbers of articles published per year (> 5) were in Environmental Health Perspective

TABLE-1
FOURTEEN CORE JOURNALS INCLUDING THE NUMBER OF ARTICLES, PERCENTAGES, SUBJECT CATEGORIES AND POSITIONS

Journal	Total publication (Rank)	Impact factor	Category	Position
Environmental Health Perspectives	94 (5.2)	5.636	Environmental Sciences	1/160
			Public, Environmental & Occupational Health	2/100
Environmental Science & Technology	74 (4.1)	4.363	Environmental Engineering	2/37
			Environmental Sciences	4/160
Toxicology and Applied Pharmacology	64 (3.5)	3.846	Pharmacology & Pharmacy	36/205
			Toxicology	6/73
Science of the Total Environment	51 (2.8)	2.182	Environmental Sciences	38/160
Journal of Environmental Science and Health Part A-Toxic/Hazardous Substances & Environmental Engineering	50 (2.8)	0.967	Environmental Engineering	24/37
			Environmental Sciences	107/160
Water Research	47 (2.6)	3.427	Environmental Engineering	3/37
			Environmental Sciences	12/160
			Water Resources	1/59
Journal American Water Works Association	36 (2)	0.605	Civil Engineering	36/89
			Water Resources	48/59
Environmental Geochemistry and Health	32 (1.8)	1.086	Environmental Engineering	19/37
			Environmental Sciences	97/160
			Public, Environmental & Occupational Health	76/100
			Water Resources	26/59
Journal of Hazardous Materials	32 (1.8)	2.337	Environmental Engineering	5/37
			Civil Engineering	1/89
			Environmental Sciences	32/160
Applied Geochemistry	31 (1.7)	1.744	Geochemistry & Geophysics	21/63
Toxicological Sciences	28 (1.5)	3.814	Toxicology	7/73
Environmental Geology	25 (1.4)	0.722	Environmental Sciences	130/160
			Multidisciplinary Geosciences	102/137
			Water Resources	42/59
Environmental Research	25 (1.4)	2.962	Environmental Sciences	19/160
			Public, Environmental & Occupational Health	18/100
Chemical Research in Toxicology	23 (1.3)	3.508	Medicinal Chemistry	6/41
			Multidisciplinary Chemistry	19/128
			Toxicology	10/73

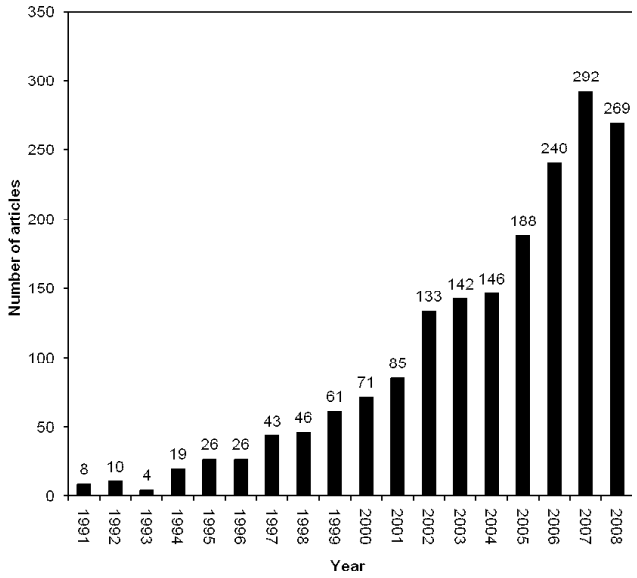

Fig. 1. Publication outputs per year for the period 1991 to 2008

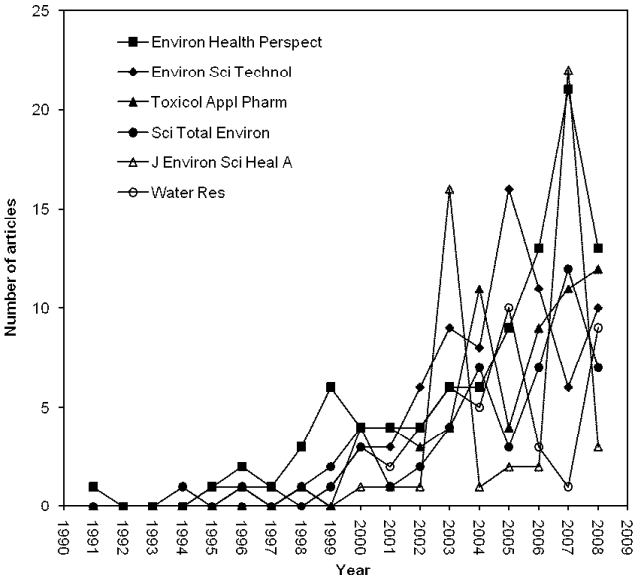

Fig. 2. Publications of the six most productive journals

in 1999. The time from 2002 to 2008 shows an increase in the number of articles published per year. In 2007 more than 20 articles were published in Journal of Environmental Science and Health Part A-Toxic/Hazardous Substances & Environmental Engineering followed by Environmental Health Perspective.

Based on the classification of subject categories in Journal Citation Report (JCR) of the ISI, the 1,809 publication output was distributed in 101 subject categories during the studied years. The three most common categories were the environmental sciences (732; 40 %), toxicology (382; 21 %) and public, environmental & occupational health (368; 20 %). Table-2 shows the ten ISI subject categories with the most publications including the number of articles and percentage of total articles. The subject categories containing 200 or above articles were statistically analyzed in Fig. 3. The number of scientific articles per category exhibited sustaining growth during the time period covered, which indicates that arsenic

TABLE-2
TEN ISI SUBJECT CATEGORIES WITH THE MOST PUBLICATIONS

Subject category	Total publication	%
Environmental Sciences	732	40
Toxicology	382	21
Public, Environmental & Occupational Health	368	20
Environmental Engineering	281	16
Water Resources	243	13
Pharmacology & Pharmacy	132	7.3
Analytical Chemistry	106	5.9
Civil Engineering	102	5.6
Oncology	82	4.5
Chemical Engineering	70	3.9

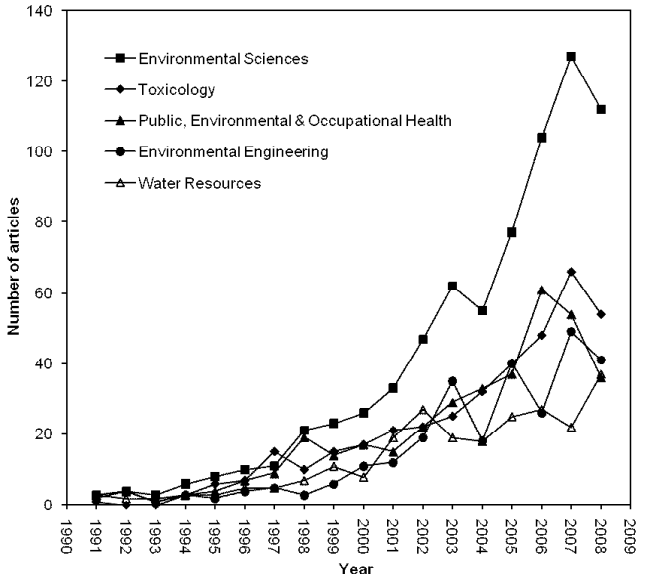

Fig. 3. Comparison the growth trends of subject categories containing 200 above articles

in drinking water related research have been steadily developing in various categories.

Distribution of source title analysis: The growth and development of research by the dissertation title analysis was primarily presented[24]. The distribution of words in article title used in different periods was applied to evaluate research trend. The title of an article always includes the information which author would most like to express to their readers, because it would be seen by all the readers at first. Table-3 listed the 30 most frequency used single words in title, which are all substantives, have been analyzed in between 1991-2008 and in 3 six-year periods, respectively. Excepted searching word " arsenic," "water," and "drinking," the title word "exposure" is used in 215 publications which ranked top one. The word " adsorption" more frequently appeared in the title, while the percentage of articles with the word increased from 0 to 4.1 %. Adsorption is one of the most used techniques in drinking water treatment. In addition, more attention was paid to West Bengal in India.

Distribution of author keyword analysis: The author keyword analysis could offer the information of research trend which is concerned by researchers. Bibliometric method concer-

TABLE-3.
TOP 30 MOST FREQUENCY SUBSTANTIVES IN THE TITLE OF ARTICLES DURING 1991-2008 AND 3 SIX-YEAR PERIODS

Words in title	TP	91-08 R (%)	91-96 R (%)	97-02 R (%)	03-08 R (%)
Arsenic	1,258	1 (70)	1 (59)	1 (74)	1 (69)
Water	422	2 (23)	3 (15)	2 (30)	2 (22)
Drinking	269	3 (15)	6 (8.6)	3 (21)	3 (13)
Exposure	215	4 (12)	4 (12)	5 (8.4)	3 (13)
Removal	196	5 (11)	11 (5.4)	4 (10)	5 (12)
Groundwater	145	6 (8)	15 (4.3)	12 (5.2)	6 (9.2)
Bangladesh	129	7 (7.1)	N/A	11 (6.2)	7 (8.0)
Inorganic	122	8 (6.7)	5 (11)	6 (7.1)	8 (6.3)
Effects	114	9 (6.3)	15 (4.3)	8 (6.6)	8 (6.3)
Human	103	10 (5.7)	49 (2.2)	6 (7.1)	12 (5.5)
Arsenite	100	11 (5.5)	110 (1.1)	8 (6.6)	12 (5.5)
Using	97	12 (5.4)	N/A	19 (4.3)	10 (6.1)
Study	96	13 (5.3)	11 (5.4)	17 (4.6)	11 (5.6)
Risk	82	14 (4.5)	8 (6.5)	25 (3.9)	14 (4.6)
Exposed	80	15 (4.4)	7 (7.5)	28 (3.4)	15 (4.5)
Cells	78	16 (4.3)	49 (2.2)	17 (4.6)	16 (4.4)
Cancer	77	17 (4.3)	15 (4.3)	8 (6.6)	30 (3.4)
Acid	73	18 (4.0)	26 (3.2)	19 (4.3)	22 (4.0)
Mice	73	18 (4.0)	11 (5.4)	29 (3.0)	18 (4.3)
Skin	71	20 (3.9)	N/A	15 (4.8)	23 (3.9)
Health	65	21 (3.6)	49 (2.2)	34 (2.5)	20 (4.1)
Chronic	64	22 (3.5)	11 (5.4)	19 (4.3)	33 (3.1)
Contamination	64	22 (3.5)	N/A	27 (3.6)	27 (3.8)
Speciation	63	24 (3.5)	110 (1.1)	19 (4.3)	31 (3.4)
Iron	63	24 (3.5)	N/A	40 (2.3)	19 (4.2)
Adsorption	63	24 (3.5)	110 (1.1)	40 (2.3)	20 (4.1)
Bengal	63	24 (3.5)	N/A	80 (1.6)	16 (4.4)
Arsenate	62	28 (3.4)	26 (3.2)	40 (2.3)	24 (3.8)
Urinary	62	28 (3.4)	49 (2.2)	32 (2.7)	27 (3.8)
Concentrations	58	30 (3.2)	49 (2.2)	23 (4.1)	34 (3.0)

TP = Total publications; R = Rank; N/A= Not available.

ning author keyword analysis can only be found in recent years[25], whereas using the author keyword to analyze the trend of research is much more infrequent[26]. The technique of statistical analysis of keywords might be aimed at discovering directions of science and prove important for monitoring development of science and programs. Examining the author keywords used during 1991-2008 and three six year periods was performance. Table-4 shows the top 20 most used author keywords. Due to Bangladesh worst affected zone by arsenic toxicity, the percentage rate of Bangladesh and groundwater in author keywords were 0 and 2.3 % in between 1991-1996 increased to 5.7 and 7.0 % (2003-2008). It can be concluded from Table-4 that groundwater and adsorption were the hot spot keywords for the authors.

Distribution of keyword plus analysis: The keywords plus provides search terms extracted from the titles of papers cited in each new article in the database in ISI. The KeyWord Plus analysis as an independent supplement, reveals the articles contents with more details. It is an additional search terms and is usually more concerned about the novel research direction than the mature direction in the field[27]. The distribution of the keywords plus with its rank and percentage in different periods was revealed in Table-5. It is clear that West-Bengal in India, Bangladesh, groundwater, sorption and iron became hot topics in recent years.

TABLE-4
TOP 20 MOST FREQUENCY USED AUTHOR KEYWORD DURING 1991-2008 AND 3 SIX-YEAR PERIODS

Author keyword	TP	91-08 R (%)	91-96 R (%)	97-02 R (%)	03-08 R (%)
Arsenic	719	1 (56)	1 (58)	1 (63)	1 (54)
Drinking water	168	2 (13)	2 (12)	2 (22)	2 (11)
Bangladesh	81	3 (6.3)	N/A	4 (5.2)	3 (7.0)
Arsenite	73	4 (5.7)	8 (4.7)	3 (5.9)	5 (5.7)
Adsorption	68	5 (5.3)	19 (2.3)	13 (2.8)	4 (6.2)
Groundwater	67	6 (5.2)	19 (2.3)	6 (4.1)	5 (5.7)
Arsenate	45	7 (3.5)	5 (7.0)	30 (1.7)	7 (3.9)
Oxidative stress	40	8 (3.1)	19 (2.3)	30 (1.7)	8 (3.6)
Speciation	39	9 (3.1)	8 (4.7)	6 (4.1)	10 (2.6)
Arsenic removal	38	10 (3.0)	N/A	8 (3.4)	9 (3.0)
Methylation	32	11 (2.5)	19 (2.3)	8 (3.4)	11 (2.2)
Urine	31	12 (2.4)	19 (2.3)	4 (5.2)	16 (1.6)
Water	26	13 (2.0)	3 (9.3)	24 (2.1)	15 (1.7)
Inorganic arsenic	25	14 (2.0)	N/A	15 (2.4)	12 (1.9)
Risk assessment	23	15 (1.8)	19(2.3)	11 (3.1)	21 (1.4)
Skin lesions	22	16 (1.7)	N/A	15 (2.4)	16 (1.6)
Arsenic speciation	22	16 (1.7)	8 (4.7)	56 (1.0)	14 (1.8)
Cancer	22	16 (1.7)	5 (7.0)	13 (2.8)	30 (1.2)
Dimethylarsinic acid	22	16 (1.7)	19 (2.3)	8 (3.4)	30 (1.2)
Arsenicosis	21	20 (1.6)	N/A	56 (1.0)	12 (1.9)
Cadmium	21	20 (1.6)	8 (4.7)	15 (2.4)	24 (1.3)

TP = Total publications; R = Rank; N/A= Not available.

TABLE-5
TOP 30 MOST FREQUENCY USED KEYWORD PLUS DURING 1991-2008 AND 3 SIX-YEAR PERIODS

Keyword plus	TP	91-08 R (%)	91-96 R (%)	97-02 R (%)	03-08 R (%)
Drinking-water	945	1 (56)	1 (29)	1 (51)	1 (59)
West-Bengal	262	2 (15)	56 (1.4)	2 (16)	2 (16)
Exposure	207	3 (12)	10 (8.2)	3 (14)	5 (12)
Bangladesh	185	4 (11)	N/A	39 (3.3)	3 (14)
Groundwater	185	4 (11)	56 (1.4)	7 (7.6)	4 (13)
Adsorption	159	6 (9.4)	30 (2.7)	9 (7.1)	6 (11)
Speciation	142	7 (8.4)	13 (6.8)	4 (11)	8 (7.8)
Contamination	138	8 (8.1)	30 (2.7)	32 (3.8)	7 (10)
India	119	9 (7.0)	N/A	5 (9.3)	9 (6.7)
Toxicity	101	10 (6)	56 (1.4)	22 (4.5)	9 (6.7)
Removal	99	11 (5.8)	18 (4.1)	37 (3.5)	9 (6.7)
Cancer	98	12 (5.8)	2 (12)	14 (6.3)	12 (5.2)
Well water	86	13 (5.1)	3 (11)	13 (6.8)	16 (4.2)
Ground-water	81	14 (4.8)	30 (2.7)	9 (7.1)	16 (4.2)
Mortality	80	15 (4.7)	3 (11)	7 (7.6)	28 (3.4)
Sodium arsenite	74	16 (4.4)	8 (10)	17 (5.5)	24 (3.7)
Water	74	16 (4.4)	18 (4.1)	15 (6.0)	19 (3.8)
Dimethylarsinic acid	72	18 (4.2)	56 (1.4)	21 (4.8)	15 (4.2)
Blackfoot disease	72	18 (4.2)	3 (11)	17 (5.5)	28 (3.4)
Cells	71	20 (4.2)	56 (1.4)	19 (5.3)	18 (4.0)
Malignant neoplasms	70	21 (4.1)	3 (11)	9 (7.1)	44 (2.8)
Sorption	69	22 (4.1)	N/A	51 (2.3)	13 (4.9)
Taiwan	67	23 (4.0)	30 (2.7)	22 (4.5)	19 (3.8)
Iron	64	24 (3.8)	N/A	85 (1.5)	14 (4.7)
Prevalence	63	25 (3.7)	N/A	22 (4.5)	24 (3.7)
6 Districts	63	25 (3.7)	56 (1.4)	6 (8.1)	52 (2.4)
Affected people	61	27 (3.6)	56 (1.4)	9 (7.1)	48 (2.6)
Metabolism	61	27 (3.6)	10 (8.2)	20 (5.0)	40 (2.9)
Calamity	60	29 (3.5)	N/A	15 (6.0)	38 (2.9)
Skin-cancer	59	30 (3.5)	30 (2.7)	26 (4.3)	32 (3.3)

TP = Total publications; R = Rank; N/A= Not available.

Data sources and case study

Historical scenario: The cases of arsenic poisoning through drinking water have been reported since long in the world history. In 1898, the cases of skin cancer were observed among population consuming arsenic contaminated water in Poland[28].

In 1937, Wyllie[29] reported that the water from some the deep wells in Rocky Mountain areas of Ontario, Canada contains large amounts of arsenic in the form of ferrous arsenate. The concentration of arsenic varies from 0.10 to 0.41 mg/L. The preliminary experiments showed that arsenic as arsenate was the primary source of arsenic in contaminated well water. One person died of arsenic dermatosis. The whole family members of the victim died was also afflicted due to this arsenic poisoning.

In 1939, Grimmet and McIntosh[30] observed and reported arsenic contamination of groundwater and the resulting effects on the health of livestock in New Zealand. Later on in 1961, high levels of arsenic were found in water from areas of thermal activity. Thermal waters in New Zealand contain up to 8.5 mg/L of arsenic[28].

In 1976, several wells in Halifax County, Nova Scotia were found contaminated with arsenic[31]. The concentration was greater than 3 mg/L. More than 50 families have been affected due to arsenic poisoning[32].

The arsenic contamination incident in well water on the south-west coast of Taiwan (1961-1985) is well known[33]. The population of endemic area was about 140,000. In the villages surveyed, the arsenic content of the well water examined, ranges from 0.01 to 1.82 mg/L. Most of the well water in the endemic area has arsenic content around 0.4-0.6 mg/L. The predominant arsenic species in the well waters was arsenite with an average arsenite to arsenate ratio of 2.6.

The chronic arsenic exposure *via* drinking water was reported in six areas of Lagunera region, situated in the central part of North Mexico with a population of 200,000 during 1963-1983[34]. The range of total arsenic concentration was 0.008-0.624 mg/L and concentration level above 0.05 mg/L was found in 50 % of the samples. Most of the arsenic was in inorganic form and arsenate was the predominant species in 93 % of the samples.

Arsenic contamination in groundwater was also reported in Monte Quemado of Cordoba province, north of Argentina[35]. The occurrence of endemic arsenical skin disease and cancer was first recognized in 1955. The total population of endemic area was about 10,000. From the observations in the Cordoba, it was concluded[36] that the regular intake of drinking water containing more than 0.1 mg/L of arsenic leads to clearly recognizable signs of intoxication and ultimately might develop into skin cancer.

During the 1980s, the endemic arsenicosis was found successively in many areas on mainland China such as Xinjiang Uygur A.R., Inner Mongolia, Shanxi, Liaoning, Jilin, Ningxia, Qinghai and Henan provinces[37,38]. The arsenic concentration in the groundwater in these affected areas was ranged from 220-2000 µg/L with the highest level at 4440 µg/L.

Present scenario: Primarily, arsenic enters into the food chain *via* more problematic inorganic forms[39]. The contamination of arsenic in groundwater depends on pH dependent adsorption to mineral surfaces (iron oxide). The mobilization mechanism of arsenic in drinking water depends on biologically mediated changes in the iron (Fe) mineralogy[40]. In some cases, reductive dissolution of Fe minerals has been shown to increase arsenic concentrations in groundwater, more commonly associated with anthropogenic activities such as landfills. Evidence of nitrate reduction promoting the presence of arsenate and ferric [Fe(III)] minerals in anoxic environments has been shown to occur in surface waters[41]. The arsenic contents in groundwater of different countries are summarized in Table-6.

TABLE-6
CONCENTRATION OF ARSENIC IN WATER OF ARSENIC AFFECTED COUNTRIES

Location	Source of arsenic	Conc. (µg/L)	Ref.
Argentina, Bangladesh, India, Mexico, Thailand and Taiwan	Ground water	100-2000	9
Southern region of Fukuoka Prefecture, Japan	Well water	29.3	17
Matiari and Khairpur districts, Sindh, Pakistan	Ground water	50-250	205
Mekong delta (Southern Vietnam and bordering Cambodia)	Drinking water	0.1-1340	206
Manikganj	Tube wells	0.25-191	207
Hungary	Deep groundwater	1-174	208
Mekong River delta	Aquifer groundwater	1300	209
Bigadic borate deposits (Western Turkey)	Ground water	33-911	210
Chakdaha block, Nadia, district, West Bengal	Groundwater	200-50	211
Prey Veng and Kandal, Cambodian	Tube well waters	0-900	212
Hetao Basin of Inner Mongolia	Groundwater	0.6-572	213
YiLan and Jhung Wei townships, Taiwan	Well water	70.32	214
Inner Mongolia	Well water	2000	215
Aksios and Kalikratia areas in Northern Greece	Groundwater	10-70	216
Central Mexico	Drinking water	2-378	217

The magnitude of this problem is severe in Bangladesh and West Bengal, India[42,43]. In West Bengal alone more than 6 million people[44] living in almost 50 % of the districts[45] are exposed to arsenic through drinking water. In recent years the evidence of groundwater contamination by arsenic has emerged in many other Asian countries including Cambodia, the Lao People's Democratic Republic, Myanmar, Pakistan[43], Nepal[46], Cambodia, Vietnam[47], a province in Iran[48]. The higher level of arsenic concentration in drinking water has been reported in Ghana where *ca.* 45 % of the total drinking water is produced from groundwater[49]. Barbu *et al.*[50] reported that along with other metals arsenic is also present in high concentration in the Jiu River, Romania.

In India, along with West Bengal, some cases of arsenic contaminated water were reported in Bihar state[46] located in the Middle Gangetic Plain. With the discovery of arsenic in groundwater in other states of India (Uttar Pradesh, Jharkhand

and Assam)[51] it appears that areas among Indian states and Bangladesh that lie on the Ganga-Meghna-Brahmaputra (GMB) plain (which is home to a population of over 450 million people and encompasses an area of 570000 km^2) might be at risk from groundwater arsenic contamination. The sources of arsenic in Ganga-Meghna-Brahamputra plain are the sediments derived from the Himalaya and surrounding mountains[52].

The late quaternary stratigraphy and sedimentation in the Middle Ganga Plain (MGP) (Uttar Pradesh-Bihar) have influenced groundwater arsenic contamination. The MGP sediments are mainly derived from the Himalayas with minor inputs from the Peninsular India therefore, the potential source of arsenic in MGP is mainly from the Himalayas. Arsenic was transported from disseminated sources as adsorbed on dispersed phases of hydrated-iron-oxide and later on released to groundwater mainly by reductive dissolution of hydrated-iron-oxide and corresponding oxidation of organic matter in aquifer[53].

The elevated level arsenic is well known to be present in aquifers utilized for drinking water and irrigation in West Bengal and Bangladesh[54]. The sediments within the aquifers are considered to be the source of the arsenic with highest concentration in the Holocene aquifer[55]. The Holocene deltaic and organic-rich surface sediments are the key indicators for arsenic risk areas[56]. The release of arsenic from the aquifer rock was strongly related to the bicarbonate concentration in the leaching solution[57]. The concentration of arsenic in aquifers is affected by electromagnetic conductivity of the soil. The concentration of arsenic is higher below finer grained and high conductivity soil[58].

The microbial Fe reduction is widely believed to be the primary mechanism of arsenic release from aquifer sands in Bangladesh[59]. Leaching of organic matter from thin silt layers could cause reducing conditions and therefore potentially be related to particularly high concentrations of dissolved ammonium ions, bicarbonate, phosphorous and dissolved organic compounds in the portion of the aquifer where groundwater arsenic concentrations are also elevated[60]. The studies on arsenic affected aquifers in the Lanyang Plain, Taiwan shows that deep aquifer has a high hazard rating and is less safe than the shallow aquifer[61]. The existence of arsenic rich (exceeds 2000 mg/kg) iron pyrite in Bengal delta sediments is responsible for arsenic release in aquifer[62]. The groundwater quality was also influenced by the uranium mining site exhibiting high levels of arsenic. The study on Turkey's largest uranium site in Koprubasi, near the city of Izmir in the Aegean region found that arsenic and uranium contamination of groundwater is directly related to the distribution of uranium ores in aquifer rocks and uranium mines[63].

The arsenic distribution of groundwater in SW Uruguay was studied by Manganelli and coworkers. Twenty-eight wells were sampled on the aquifers of Mercedes, Raigon and Chuy in five localities. The pH, specific conductivity and temperature were determined in the field. The occurring arsenic concentrations exceed the recommended threshold for drinking water of the World Health Organization (10 µg/L of arsenic) in 22 samples, with more than 50 µg/L of arsenic in two samples. The median, minimum and maximum concentrations were 0.1, 16.9 and 58.0 µg/L of arsenic, respectively. The studied aquifers present a horizontal and a vertical variation of the concentrations as a whole as well as individually. The highest values were observed in the Mercedes aquifer in the areas near the Uruguay river[64]. The distribution of arsenic in the world is shown in Fig. 4. The enrichment of arsenic in drinking water wells in south and south east Asia is generally attributed to the reductive dissolution of iron oxides[65]. While, the presence of carbonates decreased oxidation rates and arsenic release[66]. The arsenic enrichment of groundwater in the Red river (Song Hong) delta in Vietnam found concentrations of arsenic exceeding the WHO guideline. The distribution of arsenic is highly variable.

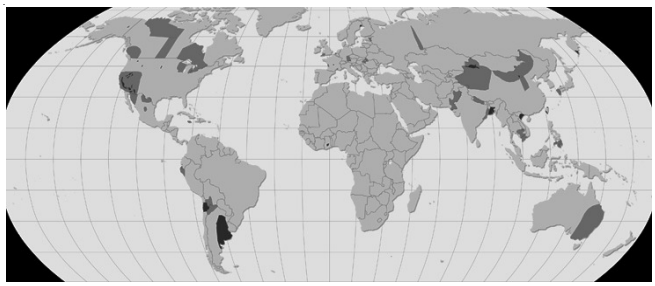

Fig. 4. Distribution of arsenic in the world water table, Dark colour high concentration, Light colour lower concentration, Source International Groundwater Resources Assessment Centre (http://igrac.nitg.tno.nl/)

Effect of toxicity: The wide human exposure to this compound through drinking water throughout the world causes great concern for human health[67,68]. Arsenic containing drinking water has been associated with a variety of skin and internal organ cancers[69]. Long-term exposure to arsenic in drinking water can lead to cancer of the liver, lung, kidney and bladder[69,70]. The higher level of arsenic in drinking water may result in an increase in childhood liver cancer mortality rate[71]. Benbrahim-Tallaa and Waalkes reported that prostate was a target for inorganic arsenic carcinogenesis[72].

The noncancerous effects of ingesting arsenic include cardiovascular diseases[73], pulmonary, immunological, neurological and endocrine (*e.g.*, diabetes) disorders[74]. Studies carried out in southwestern Taiwan showed that chronic exposure to arsenic in drinking water leads to the occurrence of pterygium, a fibrovascular growth of the bulbar conjunctival and underlying subconjunctival tissue that may cause blindness[75]. The exposure to arsenic causes testicular dysgenesis in male rabbits[76]. Arsenic exposure is responsible for a decrease in the IQ scores in children[77], children's cognitive development[78]. The environmental arsenic exposure, through drinking contaminated water, is a significant risk factor for developing liver portal hypertension, vascular shunting and portal fibrosis[79]. Arsenic is a major risk factor for blackfoot disease (BFD), a unique peripheral vascular disease that was endemic to the southwestern coast of Taiwan[80]. Arsenic induced neurotoxicity, like many other neurodegenerative diseases, causes changes in cytoskeletal protein composition and hyperphosphorylation. These changes may lead to disorganization of the cytoskeletal framework, which is a potential mechanism of arsenic induced neurotoxicity[81]. The arsenic toxicity causes respiratory complications, induced changes in the humoral as well as mucosal immune responses[82].

Guo and coworkers[83] surveyed the population using arsenic contaminated drinking water in 13 counties of Inner Mongolia, China, most of which are located in the Hetao Plain area. They observed that the exposure of population to arsenic contaminated drinking water causes hyperkeratosis on the palms or soles and some had raindrop-like hyper-pigmentation and de-pigmentation on the trunk, chronic cough and insomnia. The liver function tests showed elevated globulin levels among the population. Neurotoxicity manifesting as loss of hearing, loss of taste, blurred vision, tingling and numbness of the limbs and hypertension were significantly higher[83].

A case of cutaneous manifestations with chronic arsenicism was reported in a Chinese women residing in US but using Chinese herbal medicine for last 5 year[84]. Arsenic toxicity cases Bowen's disease, a neoplastic skin disease, considered either as an early stage or intraepidermal form of squamous cell carcinoma[85]. The chronic exposure to high concentrations of arsenic in drinking water is associated with an increased risk for developing type 2 diabetes, as it affects insulin sensitivity in peripheral tissue by modifying the expression of genes involved in insulin resistance and shifting away cells from differentiation to the proliferation pathway. In liver, arsenic disturbs glucose production, whereas in pancreatic β-cells arsenic decreases insulin synthesis and secretion and reduces the expression of antioxidant enzymes. The consequences of these changes in gene expression include the reduction of insulin secretion, induction of oxidative stress in the pancreas, alteration of gluconeogenesis, abnormal proliferation and differentiation pattern of muscle and adipocytes as well as peripheral insulin resistance[86]. Ahmad *et al.*[87] studied the pregnancy outcomes induced by arsenic toxicity in drinking water. The results showed adverse pregnancy outcomes in terms of spontaneous abortion, stillbirth and preterm birth rates were significantly higher in the exposed group females.

Among animals, exposure to pregnant mice is causative for mammalian spontaneous abortion by virtue of aberrant placental vasculogenesis and placental insufficiency[88]. Malago and Nondoli investigated the effect of sodium arsenite on rats with dextran sulfate sodium (DSS)-colitis. They concluded that sodium arsenite significantly reduces the severity of dextran sulfate sodium-induced ulcerative colitis in rats and improved the weight gain[89].

Among food crops, higher concentration of arsenic in soil is found to be responsible for Straighthead disease. It is a physiological disorder of rice (*Oryza saliva* L.) characterized by sterility of the florates/spikelets leading to reduced grain yield. With the increase of soil arsenic concentration, the severity of Straighthead increased significantly[90].

Besides its carcinogenic properties arsenic is a novel promising anticancer agent used effectively to treat acute promyelocytic leukemia (APL)[91]. The toxicity of arsenic is exploited in the antileukemia drug, arsenic trioxide commercially known as Trisenox was successfully utilized for the treatment of patients suffering relapsed acute promyelocytic leukemia[92,93].

Biomarkers of arsenic toxicity: Biomarker (or biosignature) is a substance used as an indicator of a biologic state. It is a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes or pharmacologic responses to a therapeutic intervention.

Nails and hairs are the effective biomarkers of arsenic toxicity[94-96], whereas arsenic in urine and breast milk did not cluster with water arsenic[94]. Blood arsenic is a useful biomarker only in the case of acute arsenic poisoning or stable chronic high-level exposure[97]. The genetic effects of arsenic exposure are detected from peripheral blood lymphocytes biomarker[98]. Yuan and coworkers studied the correlation of saliva arsenic with drinking water arsenic. They concluded that human saliva is a useful method for monitoring arsenic exposure[99]. Arsenic *in vitro* induced a three-fold increase in the expression of α-fetoprotein (AFP), a biomarker associated with transplacental arsenic induced mouse liver tumors[100]. Plasma biomarkers of exposure to environmental contaminants play an important role in early detection of disease. The emerging field of proteomics presents an attractive opportunity for candidate biomarker discovery, as it simultaneously measures and analyzes a large number of proteins[101]. Maternal arsenic exposure early in pregnancy negatively affects newborn birth weight and that maternal hair provides the best integrated measure of arsenic exposure[102]. Krishnamohan and coworkers[103] reported that urinary dimethylarsinic acid [DMA(V)] and porphyrin profile can be used as an early warning biomarker for chronic monomethylarsonic acid [MMA(III)] exposure before the onset of cancer. Alterations in renal hexokinase II [HK(II)] expression may be involved in arsenic induced pathological conditions involving the kidney[104].

Mechanism of accumulation and toxicity

In animals: The chronic exposure to arsenic involves a biotransformation process leading to the excretion of methylated metabolites, such as monomethyl arsenic and dimethyl arsenic, as well as the parental inorganic species (arsenite and arsenate)[105]. Cocarcinogenic mechanisms could include blocking DNA repair, stimulating angiogenesis, altering DNA methylation patterns, dysregulating cell cycle control, induction of aneuploidy and blocking apoptosis[106].

Arsenic exposure can cause immunosuppression in humans[107]. The generation of reactive oxygen species (ROS) is one of the possible mechanisms suggested for arsenic toxicity[97]. Arsenic metabolism is characterized by two main types of reactions: (1) reduction reactions of arsenate to arsenite and (2) oxidative methylation reactions in which arsenite are sequentially methylated to form mono-, di- and trimethylated products using S-adenosyl methionine (SAM) as the methyl donor and glutathione (GSH) as an essential co-factor.

The effect of exposure was studied in different animals and human beings. Arsenate is a non-functional phosphate analog that enters the food chain *via* plant phosphate transporters. Inside cells, arsenate is reduced to arsenite for subsequent extrusion or compartmentation[108]. Aggarwal *et al.*[109] studied the effect of arsenic exposure on the biological system of one day old chicks with exposure level of 3.7 mg/L of arsenic *via* drinking water for 60 days. The results do not reflect any specific type of interaction between these agents in chicken erythrocytes, but they do indicate that the co-exposure induces a lower level of oxidative stress, which is comparable to that

induced by arsenic. Cui and Okayasu[110] studied arsenic accumulation, distribution and influences on metallothionein-1 (MT-1) expression and other trace elements in various organs of rats. The rats were orally exposed to sodium arsenate. Rats received a dose of 0, 1, 10 and 100 mg/L of sodium arsenate in drinking water daily for 4 and 16 weeks. Arsenic seems to be distributed in all of the tissues. The accumulated was relatively higher in the spleen, lung and kidney compared to the liver and was much lower in skin and cerebrum. They found that high dose of sodium arsenate exposure significantly increased the concentration of copper in the kidney, but did not influence other trace elements such as zinc and manganese in the liver. The mRNA expression of MT-1 was dose-dependent increased by sodium arsenate exposure in the liver whereas it was decreased in the kidney. The results indicate that arsenic is widely distributed and significantly accumulated in various organs and influences on other trace elements and also modulates MT-1 expression in the liver and kidney[110].

The exposure of male Wistar rats to 50 mg/L of sodium arsenite in drinking water for ten months causes single-strand DNA damage in lymphocytes[97]. The addition of low doses of arsenite to the drinking water of mice resulted in marked pathologic remodeling in liver sinusoidal endothelial cells (SECs), including SEC defenestration, capillarization, increased junctional PECAM-I expression, protein nitration and decreased liver clearance of modified albumin[79]. Arsenic *in vitro* induced a three-fold increase in the expression of α-fetoprotein (AFP), a biomarker associated with transplacental arsenic induced mouse liver tumors. The exposure of maternal mice to inorganic arsenic through the drinking water induces liver tumors and aberrant gene expression in offspring when they reach adulthood[100]. Inorganic arsenic exposure also enhances pain perception and exacerbates the pathological state of inflammatory diseases in rats[111]. The effects of inorganic arsenicals on the bladder were greater when administered in the drinking water than in the diet in rats and mice[112]. The total tissue arsenic accumulation in mice was greatest in kidney > lung > urinary bladder >> skin > blood > liver. Monomethyl arsenic [MMA, *i.e.* MMA(III) + MMA(V)] was the predominant metabolite in kidney, whereas dimethyl arsenic [DMA, *i.e.*, DMA(III) + DMA(V)] was the predominant metabolite in lung[113]. Kobayashi and Hirano[114] studied the effects of endogenous hydrogen peroxide and glutathione on the stability of metabolites in rat bile. The result shows that H_2O_2 converts arsenite to less toxic arsenate, whereas glutathione (GSH) prevents hydrolysis of arsenic-glutathione (As-GSH) complexes and the generation of unconjugated toxic arsenite.

Hepatocarcinogenicity of arsenic was studied in rodents. It was found that hepatocellular carcinoma and hepatic angiosarcoma, have been frequently associated with environmental or medicinal exposure to arsenicals. Chronic exposure of rat liver epithelial cells to low concentrations of inorganic arsenic induces malignant transformation, producing aggressive, undifferentiated epithelial tumors. There are a variety of potential mechanisms for arsenical-induced hepatocarcinogenesis, such as oxidative DNA damage, impaired DNA damage repair, acquired apoptotic tolerance, hyperproliferation, altered DNA methylation and aberrant estrogen signaling[115], but one of the predominant mechanism in arsenic co-genotoxicity is inhibition of DNA repair processes. Arsenic induced DNA damage was confirmed by DNA ladder formation and confocal microscopy[116]. Monomethyl arsonous acid (MMA(III)) was the most potent inhibitor of the DNA repair[117]. The deficiency in DNA repair capacities in the hyperkeratotic individuals emerges as a prime contender for arsenic carcinogenicity[118]. Chronic inorganic arsenic exposure in mice produces liver injury and a high fat diet markedly increases arsenic induced hepatofibrogenesis[119].

The concentration of arsenic in urine has been used as a marker of exposure to inorganic arsenic. The presence of arsenic species in exfoliated bladder epithelial cells may provide a more effective tool for risk assessment of bladder cancer and other urothelial diseases associated with exposures to inorganic arsenic[120]. Higher levels of arsenic in artesian well water have been found to be associated with genitourinary cancer, especially bladder transitional cell carcinoma[121]. The evidence that arsenic induces both loss of global DNA methylation and gene promoter DNA hypermethylation has suggested that epigenetic mechanisms may play an important role in arsenic induced carcinogenesis[122]. To investigate any relationship between urothelial carcinoma and arsenite, arsenate, MMA(V) and DMA(V) a study was done by Huang *et al.*[123] on 1,078 residents of southwestern Taiwan followed for an average of 12 years. The results shows significantly higher percentages of MMA(V) and lower percentages of DMA(V) existed among the patients with urothelial carcinoma than among the healthy residents. There was a significant association between inefficient arsenic methylation and the development of urothelial carcinoma in the residents[124].

HBD-1, an antimicrobial peptide constitutively expressed in multiple tissues including epithelial cells of the respiratory and urogenital systems. The studies support HBD-1 role as a tumor suppressor gene for urological cancers suggesting that decreased HBD-1 levels may play a role in the development of cancers associated with arsenic exposure[125]. The inhalation of higher levels of airborne inorganic arsenic is a recognized cause of respiratory cancer when delivered at a higher concentration and shorter duration than when delivered at a lower concentration and longer duration[126]. The DNA damage and decreased repair ability was observed in children exposed to arsenic in drinking water in Lagunera, Mexico[127] this is because arsenic inhibits the function of key DNA repair protein poly (ADP-ribose) polymerase-1 (PARP-1) even at lower concentrations[128]. Long-term exposure to arsenic may increase the chromosome abnormality in transitional cell carcinoma[129]. The radionuclide especially α-emitting radionuclides in the environment are found to be carcinogenic. The concentration of α-activity has a positive correlation with that of arsenic[130].

In recent years increasing reports on effects of arsenic toxicity on fetal and child development have appeared. There seems to be a wide variation in susceptibility to arsenic toxicity, which is likely to be related to factors such as variation in arsenic metabolism, nutrition, host-related defense mechanisms and genetic predisposition. The main mechanisms of arsenic nutrition interactions include arsenic induced oxidative stress, which requires nutrient-dependent defense systems and arsenic metabolism (methylation) *via* 1-carbon metabolism, which requires methyl groups, folic acid, vitamin B-12 and betaine

for the remethylation of homocysteine to methionine. An efficient first methylation step in combination with a slow second methylation step seems to be most critical from a toxicological point of view. A third mode of arsenic nutrition interaction involves epigenetic effects and fetal programming *via* DNA methylation[131].

In plants: The spatial distribution of arsenic concentrations of irrigation water, soil and rice plants in a shallow tube-well command area and their relationship with Fe, Mn and P was studied by Hossain *et al.*[132]. The concentration of arsenic in 110 m long irrigation channel clearly decreased with distance from the shallow tube-well point. Such a decreasing trend was also noticed with Fe and P concentrations, but the trend for Mn concentrations was not remarkable. Hossain *et al.*[132] concluded among food crops rice could be a potential source of arsenic poisoning in people living in arsenic affected areas of Bangladesh. Mondal and Polya[133] synonymously to Hossain *et al.*[132] reported that rice is the potential sources of arsenic poisoning in people in West Bengal and the most important exposure pathway for groups exposed to lower or no arsenic in drinking water. The studies suggest that rice is more elevated to arsenic than all other grain crops tested to date, with whole grain (brown) rice having higher arsenic levels than polished (white)[134]. Kurosawa *et al.*[135] studied groundwater-soil-crop relationship with respect to arsenic contamination in farming villages of Bangladesh found the arsenic concentration in tube well water from farmyards was at least four times higher than the Bangladesh drinking water standard.

The accumulation and tolerance of the aquatic fern Azolla to arsenic was studied[136] for growing the potential fern along paddy crop to reduce arsenic transfer from soil and water to rice. It was found that *A. caroliniana* accumulate two times more arsenic than *A. filiculoides* owing to a higher influx velocity for arsenate. Arsenate uptake in aquatic macrophyte *Spirodela polyrhiza* L. occurred through the phosphate uptake pathway and by physico-chemical adsorption on Fe-plaques of plant surfaces[90]. Study was done on *Corbicula fluminea* (commonly known as Asian clam or Asiatic Clam) to assess the toxicological effects, bioaccumulation and ability to regulate arsenic. The results show that arsenic is accumulated in tissues, especially in the digestive gland and caused tissue alterations in 50 % of the organisms[137].

Sources of remediation: Reactive oxygen species (ROS) generated due to arsenic toxicity have been attributed as one of the initial signals that impart cellular toxicity, which is controlled by the internal antioxidant glutathione (GSH).The intestinal epithelium being the first barrier against such exogenous inorganic arsenic toxication[138]. A linkage was reported between arsenic methylation capacity and oxidative stress in human beings[139].

Oridonin, a natural diterpenoid purified from *Rabdosia rubescens* confers protection against arsenic induced toxicity through activation of the Nrf2-mediated defensive response. Oridonin activated the nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway at a low sub toxic dose and was able to stabilize Nrf2 by blocking Nrf2 ubiquitination and degradation, leading to accumulation of the Nrf2 protein and activation of the Nrf2-dependent cytoprotective response. Pretreatment of UROtsa cells with 1.4 μM oridonin significantly enhanced the cellular redox capacity, reduced formation of reactive oxygen species (ROS) and improved cell survival after arsenic challenge[140].

Arjunolic acid possessed the ability to ameliorate arsenic induced oxidative insult in murine brain due to its antioxidant activity[141]. It also possesses the ability to attenuate arsenic induced oxidative stress in murine liver probably *via* its antioxidant activity[142].

Studies showed that vitamin A, a naturally occurring antioxidant diminishes arsenic induced genotoxicity in human beings[143]. A study by Zablotska and co workers in Bangladesh shows that vitamin B group (thiamin, riboflavin, niacin, pyridoxine and cobalamin) and antioxidants (vitamins A, C and E) may reduce the risk of arsenic related skin lesions if taken in doses greater than the currently recommended daily amounts[144]. In mice, vitamin C (ascorbic acid) also appears to have protective effects against arsenic toxicity and oxidative stress[116]. Nutritional intervention with micronutrients many of which are antioxidants serves as a defensive system against health effects and risk of cancer[145]. In infants breast feeding protects them from arsenic poisoning even if maternal arsenic exposure is high[146]. Jaggery (or gur) a product of sugar cane juice without separation of the molasses and crystals and can vary from golden brown to dark brown in colour. It contains up to 50 % sucrose, up to 20 % invert sugars, moisture content of up to 20 % and the remainder made up of other insoluble matter such as ash, proteins and bagasse fines. The efficiency of Jaggery (or gur) to encounter the genotoxic effects induced by arsenic has been reported by Singh *et al.*[147]. A fern species of the genus Pteris in hydroponic systems is hyper accumulator of arsenic. It may be more efficient to remove arsenic from contaminated water[148]. *Pteris vittata* L. (Chinese brake fern) is effective in remediating arsenic contaminated groundwater to meet recommended standards[149,150]. Studies were done on five Argentinian medicinal plants on arsenite induced oxidative stress in Vero cells, assayed by hydroperoxide measurement. The extracts from *Eupatorium buniifolium, Lantana grisebachii, Mandevilla pentlandiana* and *Sebastiania commersoniana* prevented the formation of both aqueous and lipid hydroperoxides, but *Heterothalamus alienus* only impeded lipid ones. Therefore, antioxidant extracts are potentially beneficial and may have a protective activity against arsenite induced renal injury. Among these, the aqueous extract of *L. grisebachii* may represent the most suitable preparation for humans since the traditional usage of this plant in popular medicine is through consumption of tea[151]. Arsenic accumulation in duckweed (*Spirodela polyrhiza* L.) is good option for phytoremediation. *S. polyrhiza* L. accumulates arsenic by physico-chemical adsorption and *via* the phosphate uptake pathway when arsenate was added to the solutions. The results indicate that *S. polyrhiza* L. would be a good arsenic phytofiltrator[152].

Andrographis paniculata (commonly referred to as 'kalmegh') a traditional Indian and Chinese herbal medicine has a protective role in arsenic toxicity[153].

Natural polyphenols present in tea serve as excellent antioxidants. Tea afforded efficient reduction of arsenite induced DNA damage in human lymphocytes. Tea also quenched the excessive production of reactive oxygen species by arsenic, reduced the elevated levels of lipid peroxidation and increased

the activity of antioxidant enzymes such as catalase, superoxide dismutase and glutathione peroxidase. Furthermore, tea enhanced recovery of DNA damage. It is speculated that the antioxidant potential and repair-inducing capacity of tea might help in combating the severe genotoxic effects induced by arsenic in the human population[154].

Curcumin, an active ingredient of turmeric, a common household spice, which is a rich source of polyphenols. This compound has been extensively studied as a chemo-preventive agent against many types of cancer. It was observed that DNA damage induced by arsenic could be efficiently reduced by curcumin and the effect was more pronounced when lymphocytes were pre-incubated with curcumin prior to arsenic insult. Arsenic caused DNA damage by generation of reactive oxygen species (ROS) and enhancement of lipid peroxidation levels. Curcumin counteracted the damage by quenching ROS, decreasing the level of lipid peroxidation and increasing the level of phase 11 detoxification enzymes like catalase, superoxide dismutase and glutathione peroxidase. Curcumin also enhanced the DNA repair activity against arsenic induced damage. The expression of polymerase, a repair enzyme, was found to be highly elevated when arsenite induced damaged cells were allowed to repair in presence of curcumin[155].

The dietary organoselenium blocked the cancer enhancement effect of arsenic on mice[156]. Studies showed that co-administration of antioxidants (ascorbic acid and α-tocopherol) to arsenic exposed rats showed a substantial reduction in the levels of arsenic induced oxidative products of protein and DNA[157]. Aqueous garlic (*Allium sativum* L.) extract can be a potential protective regimen for arsenic mediated toxicity[158]. Allium-root MN assay is a simple, efficient and reproducible method for the genotoxicity monitoring of arsenic water contamination[159].

The lower serum selenium status (< 50 μg/L) is significantly correlated to the arsenic associated skin lesions in the arsenic exposed population. The accumulation of arsenic and its inhibition to be biotransformed to dimethyl arsenic occurred in human due to chronic exposure of low selenium status[123].

The efficacy of an aqueous extract of *Centella asiatica*, a small herbaceous annual plant of the family Mackinlayaceae or subfamily Mackinlayoideae of family Apiaceae was studied in the depletion of arsenic and in the recovery of a few altered biochemical variables in arsenic pre-exposed rats. Treatment with aqueous extract of *Centella asiatica* provided significant protection against δ-aminolevulinic acid dehydratase (ALAD), glutathione (GSH) and thiobarbituric acid reactive substance (TBARS) levels[160].

Treatment techniques: There are several types of treatment methods such as reverse osmosis, ultra-filtration and ion exchange which can be used for the removal of arsenic. Distilling the water can also be used to remove arsenic. Nanofiltration (NF) is a promising drinking water treatment technology for arsenic removal. However, most of the research on nanofiltration treatment of arsenic has used synthetic water[161]. Photochemical oxidation of arsenite by vacuum-UV lamp irradiation was successfully carried out by Yoon and coworkers[162]. Pal *et al.*[163] reported the removal of arsenic from drinking water by chemical precipitation with the removal efficiency of 91-92 % in synthetic feed water. Arsenic was removed effectively by polyacrylonitrile-based ultrafiltration (UF) membrane[164]. Hsieh and coworkers reported electro-ultrafiltration process for the removal of arsenic from groundwater[165]. Electro-removal process was used by Maldonado-Reyes and coworkers for the removal of arsenic[166]. Arsenic removal by coagulation-with aluminum, iron, titanium and zirconium was reported by Lakshmanan *et al.*[167]. Removal of arsenite from water could be achieved by coagulation with alum[168]. Constructed soil filter (CSF) was used by Nemade *et al.*[169] for the removal arsenic and iron from water. In CSF arsenite is oxidized to arsenate by media *via* natural oxidation and subsequently, arsenic is co-precipitated with iron. Nanosorbents like ferric-entrapped γ-alumina[170] have been used successfully for the removal of arsenic. Activated siderite-hematite column filters were used for sequestering of arsenic species.

In the recent years, a new class of materials, inorganic/polymeric hybrid adsorbents, stands out as being very effective in removing trace concentrations of arsenic from contaminated groundwater. The inorganic component, hydrated ferric oxide (HFO) particles, very selective toward both arsenite and arsenate species is irreversibly dispersed within a polymeric support using a chemical/thermal treatment. The efficiency of the hybrid adsorbent materials depends on three factors: the amount of adsorbent component (HFO), its dispersion and the accessibility to the adsorbent surface of HFO particles[171]. Cheng *et al.*[172] studied the removal of arsenate from aqueous solution by bone charcoal, reporting that adsorption is pH and dose dependent. A biomass derived from the plant *Momordica charantia* has been found to be very efficient in biosorptive removal of arsenite from drinking water[173]. The live and pretreated biomass of *Aspergillus fumigatus* was effectively used for the biosorption of arsenite from aqueous solution[174]. Fan *et al.*[175] had reported a new adsorbent developed from waste ash resulting from municipal solid waste and coal co-combustion power plant for the removal of arsenate from aqueous water. The use of aminated polyacrylonitrile fibers for the adsorption of arsenate was reported by Deng *et al.*[176] with very high adsorption capacity (256.1 mg/g). The chemically modified maize cobs waste biosorbent, modified *Aspergilus niger* biomass[177] was effectively utilized for the biosorption of arsenic[178]. The removal of arsenic species, such as arsenite and arsenate, from water and industrial wastewaters by molybdate-impregnated chitosan beads (MICB) in both batch and continuous operations was studied by Chen *et al.*[172]. The results indicate that MICB favour the adsorption of both arsenate and arsenite. The optimal pH value for arsenite and arsenate removal was 5.

Several other non-conventional adsorbents like activated alumina[179], Iron-modified granular activated carbon (GAC), zero-valent iron (ZVI)[180], granular ferric hydroxide (GFH)[181,182], titanate nanofibers[183], hydrous ferric oxide incorporated onto granular activated carbon with phenol formaldehyde resins coating[184], modified activated carbon[185], polyvinyl pyrrolidone K25 coated cassava peel carbon[186], iron-oxide coated sands[129], Iron oxide-coated fibrous sorbents[187], resin/iron oxide hybrid media[188], Alum-impregnated activated alumina (AIAA)[189], laterite iron concretions[190], cationic surfactant modified powdered activated carbon[191], Atlantic Cod fish scale, chicken fat, coconut fibre and charcoal[192], chitosan-coated biosorbent[193],

weak-base anion exchange fibrous adsorbent[194], untreated laterite[195], iron-modified light expanded clay aggregates[196], untreated powdered eggshell[197], porous ceramic membranes[198], ferric activated carbon composites[199], alumina-modified zeolite recovered from fly ash[200] natural siderite[201], laterite soil[202], modified clinoptilolite-heulandite rich tuffs[203], untreated dolomite powder[204], manganese dioxide-coated sand[16] have been reported for the removal of arsenic and its derivatives from water.

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