1.0 INTRODUCTON

Arsenic is the element invented by Albertus Magnus approx 1250 CE. Arsenic was especially popular as a poison in the 17th and 18th era and renowned as the 'Inheritance Powder' for the ubiquity of its use in disposing of spouses or relatives to fulfill own guilty. Arsenic is the element, in native language is called "SENCO BISS" that has the symbol "As", having comprises both metallic and non-metallic nature generally termed as a metalloid and it sublimates at 616^0C. In periodic table arsenic possesses in Group-V (b) along with antimony and bismuth containing atomic number 33, atomic weight 75 and electronic configuration $1s^2$ $2s^2$ $2p^6$ $3s^2$ $3p^6$ $3d^{10}$ $4s^2$ $4p^3$ [**Hsueh et al., 1997; WHO, 2001**].

During solid state the salt of As^{5+} and As^{3+} may be non-toxic or mildly toxic but in aquatic state arsenite ($As^{3+)}$ is 5- 10 times more soluble and also more toxicant than that of arsenate (As^{5+}) [**Ashan et al., 2006; Klaassen, 1990**].

Profusion of arsenic in the earth's layer, it is 20 times more than silver and is frequently associated with the ores of some metallic substance like Au, Ag, Cu, Pb, Zn, Fe, Ni and Co. Sodium arsenite ($NaAsO_2$), are generally more powerful toxicant than pentavalent (As^{+5}) arsenical forms such as Na_2HAsO_4 (sodium arsenate), As_2O_5 (arsenic pentoxide) and $Ca_3(AsO_4)_2$ (calcium arsenate) [**Armstrong et al., 1984; Chen et al., 2003**].

Due to some beneficial roles, arsenic is used commercially and industrially as alloying constituent in the production of transistors, lasers and semiconductors. Not only that but also this element is abundantly used in the manufacturing of paper, glass, pigments, textiles, metal adhesives and wood preservatives and to a small quantity, as pesticides. Organo-arsenical compounds (arsanilic acid and its

derivatives, roxersone etc.) are used as food additives for better growth of poultry and swine. Arsenic is used as a common medicine in homeopathy also [**Zadorozhnaja et al., 2000**].

Populations can be affected via air, water, soil and food. Profusely arsenic containing drinking water outbreak the globe with significant exposures noted in Bangladesh, India, Taiwan, Mexico, China, Chile, Argentina, Europe and some extent of Northern America. In India numerous places of West Bengal and wide areas of eastern part of Tripura, arsenic contaminated ground water is a warning to the public health and future prospects of agriculture and industries in the affected areas. WHO (World Health Organization) has adopted a conditional guideline for tolerable limitation of arsenic in ingesting water is 0.01 ppm. (0.01 mg/ Lt) whereas in India the level is 40 times more of this recommended safe limit and even at places as high as 96 times of that [**WHO, 1981; Franzblau and Lilis, 1989; Chowdhury et al., 2000**].

Hypothetically it can be noted that arsenic containing sulfide minerals (arsenopyrite) or their alterations products had been transported in the geologic past from some ancient volcanic belt such as the foot hills of Himalayas and deposited with the alluvium in the Bengal basin which once occupied the whole of the southern and the central parts of West Bengal and Bangladesh. These extraneous arsenic minerals buried under the alluvium of Bengal delta are seemed to be responsible for arsenic contamination problem [**Roy & Saha, 1999**]. Most experts agree that the prime resource of arsenic in underwater is geological rather than others [**WHO, 2001; Jakariya et al., 2005; IRAC, 2004**].

Strongly poisonous methylated arsenic compounds are used in pesticides eg. monosodium methyl arsenate, dimethyl arsenic acid, disodium methyl arsenate or cacodylic acid. These types of pesticides are rapidly used in agricultural field and thus, it severely pollutes the surface soil as well as water [**WHO, 2001; Acharya et al., 2000**].

Organic form of arsenic occurs in a variety of organisms like as plants, crabs, fishes and creatine of human body etc. The process of biomethylation of inorganic arsenic increases the proportion of organo-arsenic, which is frequently absorbed by plants and animals with arsenic contaminated food and water. Therefore, the arsenic content of soil and water is reduced. However, the unabsorbed parts of the organo-arsenic being toxic pollutant of the soil and water [**Vather & Concha, 2001; NRC, 2001**].

Inorganic arsenic is powerful toxicant rather than organo-arsenic which is found in trivalent and pentavalent state in nature. Both soluble forms of arsenical compounds are quickly and profoundly absorbed from the GI tract (gastrointestinal) and biomethylation occurs in liver by enzymatical and non enzymatical methylation process. The end products of ingested arsenic are monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) which excrete from the body through urine [**Shen et al., 2003; Chattopadhyay et al., 2002**]. DMA is able to form ROS (reactive oxygen species) by reacting with molecular oxygen and the resulting metabolites are dimethylarsenic radical and the dimethyl arsenic peroxyl radical [**Tabacova et al., 1992**; **Mazumder, 2005**]. Inorganic arsenic has been expressed to inhibit several antioxidant enzymes in the body, such as glutathione, glutathione peroxidase, thioredoxin reductase, and superoxide dismutase. The accumulation of ROS,

hydroxyl radicals, superoxide radicals and hydrogen peroxides exhibit anomalous gene expression at little concentration and lesions of proteins, lipids and DNA at high concentrations which ultimately provoke to cellular death [**Brinckman et al.,1977; GuhaMajumdar et al., 2010; Maiti et al., 2012**].

The chronic arsenic induction is impaired of immense health distress as it triggers for the amplified the risk of various disorders such an such different types of skin pigmentation, diabetes mellitus, cardiovascular abnormalities, nephrotoxicity and neurotoxicity. Chronic ingestion of arsenic modulates the liver function and promotes hepatotoxicity [**Maiti et al., 2012**]. Few studies explored that the induction of arsenical compounds promotes carcinogenicity mainly cancer of the lungs, skin and bladder after the chronic exposure to arsenic. In long term exposure of arsenic reproductive system is also affected where male reproductive system is affected by alteration of steroidogenesis, disruption of testicular tissue, arrestation of spermatogenesis etc [**Shukla & Pandey, 1984; Chattopadhyay et al., 2000**]. Long term arsenic exposure resulted deformity of thymus gland in pregnant mice and offspring also. [**Skalnaia et al., 1995**]. Reproductive disturbances in women, along with the alteration of normal pregnancy [**Ahmad et al., 2001**] along with unwanted abortion [**Chattopadhyay et al., 1999; Rahman et al., 2009; Yang et al., 2003**] are noted in Bangladesh, Ukraine and Taiwan and owing to utilization of arsenicated water. Arsenic has also adverse effect on fetal growth directly and also may inhibit the transportation of nutrient to the fetus by damaging the placental tissue via oxidative stress [**Chattopadhyay & Ghosh, 2010**]. Sodium arsenite can affect on the hypothalamico-pituitary-gonadal axis and resist the natural production of follicles by inhibiting the plasma FSH and LH levels [**Chattopadhyay et al., 1999**]. The adverse effect is noted on hypothalamico-pituitary-adrenal axis in arsenic

affected rat due to low level of gonadal steroidogenesis and elevations of the ACTH from the adenohypophyces that promotes the hypertrophy of the adrenal gland and increases the synthesis Δ^5,3β HSD, plasma corticosterone [**Jana et al., 2006; Chattopadhyay & Ghosh, 2010**].

Few drugs are used clinically for treating acute and chronic poisoning of arsenic such as calcium disodium EDTA (Ca-Na_2EDTA), D-penicillamine, British antilewisite (BAL) and Meso 2,3 dimercaptosuccinic acid (DMSA) [**Inns et al., 1990; Flora et al., 2007**]. Some antioxidants like as vit-C, vit-E, selenium and reduced glutathione (GSH) [**Chattopadhyay & Ghosh, 2010; Maiti & Chatterjee, 2001**] and hormone such as HCG (human chorionic gonadotrophin) [**Chattopadhyay & Gosh, 2010**] are used in rat model for therapeutic purpose on female reproductive system. Recently we have established the ameliorative efficacy of *Moringa oleifera* seed and extract of *Embelica* (amla) fruits on arsenic intoxicated liver [**Chattopadhyay et al., 2011; Maiti et al., 2014; Mishra et al 2009**].

Vit-B_{12} facilitates erythrocytes production and increases spermatozoids in semen [**Watanabe et al., 2003**]. Loss of libido, incontinence, cervical dysplasia, infertility, menoorhagia, dysfunctional uterine bleeding is occurred in vit-B_{12} deficiency [**Pongchaidecha et al., 2004**]. Folic acid is essential for fertility in both male and female. Oocyte maturation, implantation, placentation are hampered in deficiency of folic acid [**Scholl & Johnson, 2000; Ebisch et al., 2007**]. Folic acid prevents the embryonic neural tube defects, obesity and megaloblastic anemia [**Lam et al., 2009; Shaw et al., 1995**]. Folic acid and Vit-B_{12} play a decisive role on the obstructing the breakage of chromosome and hypomethylation of DNA. This incident is occurred when Vit-B_{12} concentration is diminished due to reduction of methionine synthase

action, lesser extent the SAM (S-adenosyl methionine) which may comprises diminution of the DNA methylation and caused the reason unavailability during the transformation of dUMP to dTMP [**Fenech et al., 1997; Hughes & Ong, 2000**]. The most comprehensible elucidation for the chromosome breakdown upshot of lower folate concentration is immense uracil incorrect addition into DNA resulted mutagenic lesion which promotes DNA strands braking. In vivo studies showed that scarcity of Vit-B_{12} along with higher level of plasma homocysteine is extensively interrelated with increasing the of micronuclei production. This homocysteine can remethylate by folic acid, Vit-B_{12}, and chorine to back methionine which produce SAM to reduce arsenic in its trivalent state to MMA-DMA by methylation reaction [**Sohn et al., 2003; Gamble et al., 2007**].