Defence Life Science Journal, Vol. 4, No. 2, April 2019, pp. 122-129, DOI : 10.14429/dlsj.4.12766

REVIEW PAPER

Nutritional Intervention during Chemical, Biological, Radiological, Nuclear Environments: A Dietary Perspective

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ABSTRACT

The future war scenario is based on use and applications of various conventional and non-convectional agents which includes weaponised or non-weaponised chemical, biological, radiological, nuclear (CBRN), toxic industrial materials, direct energy devices/ weapons, and or high yield explosives. These include nerve agents, blood agents, vesicants or skin blistering agents, lung irritants, asphyxiants or choking agents. Biological weapons are basically disease causing microorganisms and other replicating entities including viruses, infectious nucleic acids and prions. These agents have ability to infect host and are highly virulent, pathogenic and dangerous in nature. The interface between ammunitions and above agents is soldier whose physical and mental health is affected as enough precautionary measures are not adopted. The reducing environment thus created has various agents which enter into exposed body and lead to mild to serious damage to various vital parts of the human body. As food is important component for survival and intrinsic to basic human nutrition and health, therefore, it is imperative to develop certain kind of a wholesome meal system which can be consumed by the soldiers tasked with combating CBRN situations during such operations. Such meals can be in the form of solid or liquid type and packaged in suitable delivery system, compatible and amenable with the CBRN suit. Food can be contaminated during CBRN conditions by coming in direct or indirect contact with CBRN agents. Therefore, the food materials to be used under such conditions need to be protected in suitable coverings as consumption of contaminated food can be lethal. Designer meal for CBRN environment is not only suitable for soldiers but also to all human interface dealing with similar scenario *viz.* the low intensity conflicts and surgical operations, nuclear submarines, cosmonauts, pilots, individuals handling radiation equipment and patient undergoing chemotherapy for cancer.

Keywords: Chemical; Radiological; Biological; CBRN meal; Protection

1. INTRODUCTION

The technological advancement in science has opened entirely new avenues for every spheres of life viz. information technology, pharmaceutical, food, defence etc. The national security for any nation is of prime concern and this is why the forthcoming war patterns indicate the use of both conventional and unconventional weapons which are deadly threat to the mankind. It may be in form of a chemical, biological, radiological and or nuclear (CBRN) entity which commits to severely affect the whole humanity[1,2]. In such scenario, the fighting soldiers and the exposed population must have proper and enough defence measures for safety of individual inclusive of physical, biological, and psychological protection[1-3]. Combat feeding of troops under varied climatic, terrain and weapon platform conditions is the highlight and mainstay of R&D programmes of Defence Research and Development Organisation (DRDO) in general and Defence Food Research Laboratory (DFRL) in particular. Damages to biological system by ionising radiation are either by directly affecting bio-macromolecules or by generation of highly reactive free radicals. Free radicals cause oxidative damages to bio molecules like lipid, protein and DNA such as single strand double strand breaks and DNA-DNA and DNA-Protein cross linkage etc. Rate of damage also increases in a dose dependent manner, repair mechanism of cell will try to resolve situation, but most of them will be result in unrepaired or mis repaired stage that will lead to mutation or cell death[4]. Many studies are going on for the development of radio protectors to save our biological system from the harmful effects of radiation. That resulted in development of a number of compounds of synthetic origin such as vitamins, glycosides, nucleic acid derivatives and phosphorothioates such as amifostine. Radio protectors action can be summarised as suppression of free radicals, detoxifying reactive species and enhancing action of superoxide dismutase prostaglandins interleukins etc. stimulating DNA repair and suppressing cell division[5].

But still problems persist in form of fewer efficacies and associated toxicity with their effective doses. As an alternative source many plants have been studied and proved for their radio protective efficiency. Studies are available for the radio protective properties of plants such as *Podophyllum hexandrum*, *Spirulina plantensis*, *Chlorella vulgaris*, *Centella asiastica*,

Received : 07 March 2018, Revised : 18 January 2019
Accepted : 19 February 2019, Online published : 11 April 2019

Tinosora cordifolia etc. Plants with active constituents such as silibnin, caffeic acid, thymol, phenylpropanoids phenyl esters, phycocyanin, chlorogenic acid, curcumin lycopene, gingerol, quercetin, resveratrol, orientin, vicenin, vitamin C and vitamin E, are reportedly shown radioprotective properties properties[6,7]. Major advantage of natural compounds are their less toxicity when they are administered before or after irradiation shows protective actions[8]. Several plant based compounds are already using widely for treatment of cancer in clinical field e.g. Taxol, vinblastine, vinca alkaloids, topotecan and vincristine[9]. This review elucidates a general understanding of nutritional interventions and their role in reducing the ill effects of radiation on the soldier exposed to CBRN scenario.

2. CBRN ENVIRONMENT

An apex body entitled ONTARIO explains CBRN as weaponised or non-weaponised chemical, biological, radiological and nuclear materials that can cause great harm and pose significant threats in the hands of terrorists. Weaponised materials can be delivered using conventional bombs (e.g., pipe bombs), improved explosive materials (e.g., fuel oil-fertiliser mixture), and enhanced blast weapons (e.g., dirty bombs)[2,3]. Non-weaponised materials are traditionally referred to as dangerous goods (DG) or hazardous materials (HAZMAT) and can include contaminated food, livestock, and crops. An accidental CBRN incident is an event caused by human error or natural or technological reasons, such as spills, accidental releases, or leakages. These accidental incidents are usually referred to as DG or HAZMAT accidents. Outbreaks of infectious diseases, such as SARS, or pandemic influenza are examples of naturally occurring biological incidents[10-11].

3. EXPOSURE AND HEALTH IMPLICATIONS

There are multiple harmful effects of radiation, and many of them go unnoticed in the body. A low level exposure can lead to major digestive imbalance, blood alteration and even the destruction of many cellular structures in the body's key organs and tissue systems. Common signs of low level radiation exposure include symptoms such as fatigue, headaches, nausea, scalp tenderness, scalp discoloration, and dry/itchy skin[12,13]. In extreme cases, low exposure of radiation may also cause brain damage, memory problems, mood changes, and reduced listening capacities, psychomotor abilities, and information processing times. Large amounts of radiation exposure can have devastating consequences such as bloody vomit, hair loss, nerve damage, blood vessel destruction, seizures and, with prolonged strong exposure, can even lead to death[13-16]. Our circulatory system is also vulnerable to radiation. Even very low level of radiation exposure reduces lymphocytes in the blood. When lymphocytes are lowered, we are more likely to get infections, and what is known as mild radiation sickness. Symptoms are flu-like and may increase the likelihood of developing leukemia and lymphoma in future. The reproductive system is also vulnerable to exposure. Long-term radiation exposure can even lead to sterility, birth defects, and still-births[13-17].

Ionising radiations either directly affects the bio-macromolecules and cause damage or it will generate free radicals by reacting with smaller molecules like water. Reaction proceeds in a dose dependent manner and self defence mechanism of cells fail when dose goes high. Reactive oxygen species generated as a result of radiolysis includes hydrated electron (e_{aq}^-), hydrogen radical (.H), hydroxyl radical ($\cdot$OH), peroxyl radical($ROO\cdot$), superoxides (O^{2-})[18]. Free radicals react with cellular structures like DNA, lipid membranes, and proteins cause's damage. Self defence mechanism of cells will try to mitigate these free radicals by using enzymes such as Glutathione peroxidase reduces hydroxyl radicals and generates water, superoxide dismutase converts superoxide radicals into hydrogen peroxide and later catalase reduces them to water. But when these radicals are produced at higher rate cells will not be able to control their production and get injured. Direct effects will result in single and double strand breaks, cell try to repair these damages by a series of enzymatic reactions; either it will result in successful repair or to induce apoptosis[19]. Suppression and damages to the haematopoietic system is one of the most dangerous consequences of radiation exposure. Ionising radiation can affect directly or indirectly haematopoiesis at various levels such as stem cells, blood cells or progenitor cells etc. Directly it will cause damage to stem cells or progenitor cells and indirectly it can interfere with the communication pathways between the cells and the microenvironment. Radioprotective compounds from herbal sources can stimulate generation of haematopoietic elements thereby reduce the harmful effects of radiation. Thus, nuclear accidents results in a massive destruction to the humanity. When exposed to irradiation all the systems controlling growth and maintenance of the cell get damaged so that cell will not be able to function normally. So that an ideal radio protector should improve wound healing activity of the cells so that they can recover fast. Mechanism of wound healing includes mainly three phase namely inflammation, proliferation and remodelling.

4. DIETARY SUPPLEMENTS AND RATIONALE

Certain foods play crucial role in protecting the exposed body against radiation and these facts came out of the various studies carried out after Chernobyl disaster as shown in Table 1. These are plant foods *viz.* fruits and vegetables which have cancer fighting active principal compounds. In a study, the Swedish government has measured the residual radiation level in food following the Chernobyl disaster and mentioned that animal foods such as meat, fish, and dairy products have higher amount of radioactive substances than the plant foods such as cereals, pulses, fruits, and vegetables as they poorly absorb radiation[20]. The animal tissues are more receptive of radioactive doses than the plant matrix[21].

The natural presence of phytochemicals inclusive of fibers, antioxidants, and pigments in foods provide them the antioxidant activity necessary to fight against cellular damage caused by free radicals formed during radiation exposure. Dietary fibers from lemon peel and beetroot do possess radio-protective properties and these fibers in concentrated form may be used to eliminate the nuclides and radioactive substances. Pectin naturally present in many fruits do provide protection from radiation in particular from Cs-137. A study evaluating

Table 1. Dietary supplements for protection from radiation exposure

Group	Nominations
Salts	Potassium Iodide It saturates the thyroid gland with iodine by competing with radioactive iodine[44].
Phytochemicals	Resveratrol, Quercetin, Epigallocatechin gallate, Isoflavon (genestein), Curcumin, N-acetyl cysteine (NAC-Sulphur containing compounds), Coenzyme Q_{10}, lipoic acid[43].
Herbs and Algae	*Ginkgo biloba*, Ginseng, *Spirulina*, *Chlorella*[47].
Enzymes	Superoxide dismutase (SOD), Catalase, Bowman-Birk inhibitor[45].
Micro elements	ACE Vitamins, Selenium, Zn, and Mg[46].

30,000 atomic bomb survivors in Hiroshima and Nagasaki found that the population heavily fed with fruits and vegetables had 13 per cent less risk of death from cancer and similar diseases. Sulfur containing antioxidants present in cruciferous vegetables such as broccoli, kale, and cabbage do protect from radiation exposure as they have high detoxifying properties[22].

The foods with high antioxidant activity and water soluble vitamins are highly effective in combating the stress and the damage caused due to exposure in CBRN environment[23]. Certain studies showed that naturally colorful fruits and vegetables juices boost non-specific immunity and helps in rejuvenating the body from the detrimental effect of CBRN environment. Prolonged exposure and high dose facing results into mutagenic effects of the radiation leads to benign and malignant cancers in the exposed individuals, many green leafy vegetables have active phytochemical principals that can cope up with these after affects. *Murraya koenigii* (curry) leaves was evaluated for its broad-spectrum antioxidant and anti-mutagenic activities and found quite effective. Antioxidant, anticarcinogenic, and anti-inflammatory properties of pomegranate constituents have been well studied and it established the fact that these are very effective in the treatment and prevention of cancer, cardiovascular disease, diabetes, dental conditions, erectile dysfunction, bacterial infections and antibiotic resistance, and ultraviolet radiation-induced skin damage. Phytochemical analysis by HPLC, LC-MS and total phenolic content revealed high content of ellagitannins which might be responsible for promising antioxidant and anti-mutagenic activities of *P. granatum* peel extract.

Antioxidant and anti-mutagenic potential of Guava (*Psidium guajava)* leaf extracts was also explored in previous studies. Guava contains high amount of phenolics responsible for broad-spectrum anti-mutagenic and antioxidant properties *in vitro* and could be potential candidates to be explored as modern phyto-medicine. Consumption of carotenoid-rich (lutein, zeaxanthin, beta-carotene) foods even for a short period of time gives protection against oxidative stress. The results obtained from the study suggest that the protective role is not specifically related to carotenoids. However, they may contribute together with other substances present in plant foods such as spinach, tomato etc., to lymphocyte resistance to oxidative damage. Lycopene acts synergistically, as an effective antioxidant against LDL oxidation, with several natural antioxidants such as vitamin E, the flavonoid glabridin, the phenolics rosmarinic acid and carnosic acid, and garlic[24]. Microalgae are a potential novel source of bioactive molecules, including a wide range of different carotenoids that can be used as nutraceuticals, food supplements, and novel food products. The potential of carotenoids from marine microalgae can be used as therapeutics to treat or prevent oxidative stress-related diseases[25,26]. It is imperative to understand that the ascorbic acid, tocopherol, β carotene etc., have protective role against γ-radiation induced DNA damage in human lymphocytes. The radio-protective action of antioxidant Vitamins C, E, and beta-carotene were dependent upon their concentration as well as time and sequence of application[27] as shown in Table 1.

5. MODUS OPERANDI OF ANTI-INFLAMMATORY AND ANTIOXIDANT AGENTS IN TARGETING RADIATION INDUCED AGENTS

Cyclooxygenase-2 (COX-2) is an enzyme induced by a variety of factors such as tumor promoters, cytokines, growth factors and hypoxia. It is involved in metabolic conversion of arachidonic acid into endoperoxides which are used to synthesise prostaglandins, prostacyclin, or thromboxanes. The radiation exposure leads to excessive production of COX-mediated eicosanoids such as prostaglandins; thromboxane and 5-lipoxygenase (5-LOX) mediated leukotrienes. Eicosanoids serve as cell signalling molecules that are significant mediators of immune responses. The increased levels of prostaglandins and thromboxane, and thus an inflammatory state in the tissue, can arise within hours and persist up to weeks after irradiation in a wide range of organs and tissues. Traditional non-steroidal anti-inflammatory drugs (NSAIDs) exhibit analgesic and antipyretic effects by blocking COX-derived prostaglandin formation, with less adverse effects involving the gastrointestinal tract and reproductive system. Prostaglandins production in inflamed tissue down-regulates inflammation-related pathological symptoms such as pain and swelling on administration of COX-2 specific inhibitors. Natural antioxidants such as curcumin[28], asymmetrical indole curcumin analogs such as *N*-(3-(3-1*H*-indole-3-yl)acroyl)phenyl)-4-fluorobenzamide, pyrazole and isoxazole[29], resveratrol, *trans*-3,5,4′-trihydroxystilbene[30], flavocoxid, an extract containing a mixture of catechin and baicalin, cardamonin[31], flavones hesperidin and its aglycon hesperetin[32], isorhamnetin, an antioxidant 3′-*O*-methylated metabolite of quercetin and furan L[33] had served as leads for development of antioxidant COX-2 inhibitors. Naturally occurring chromones such as stellatin derivatives[34], 2,6-Di-*tert*-butyl-4-thiomorpholin-4-

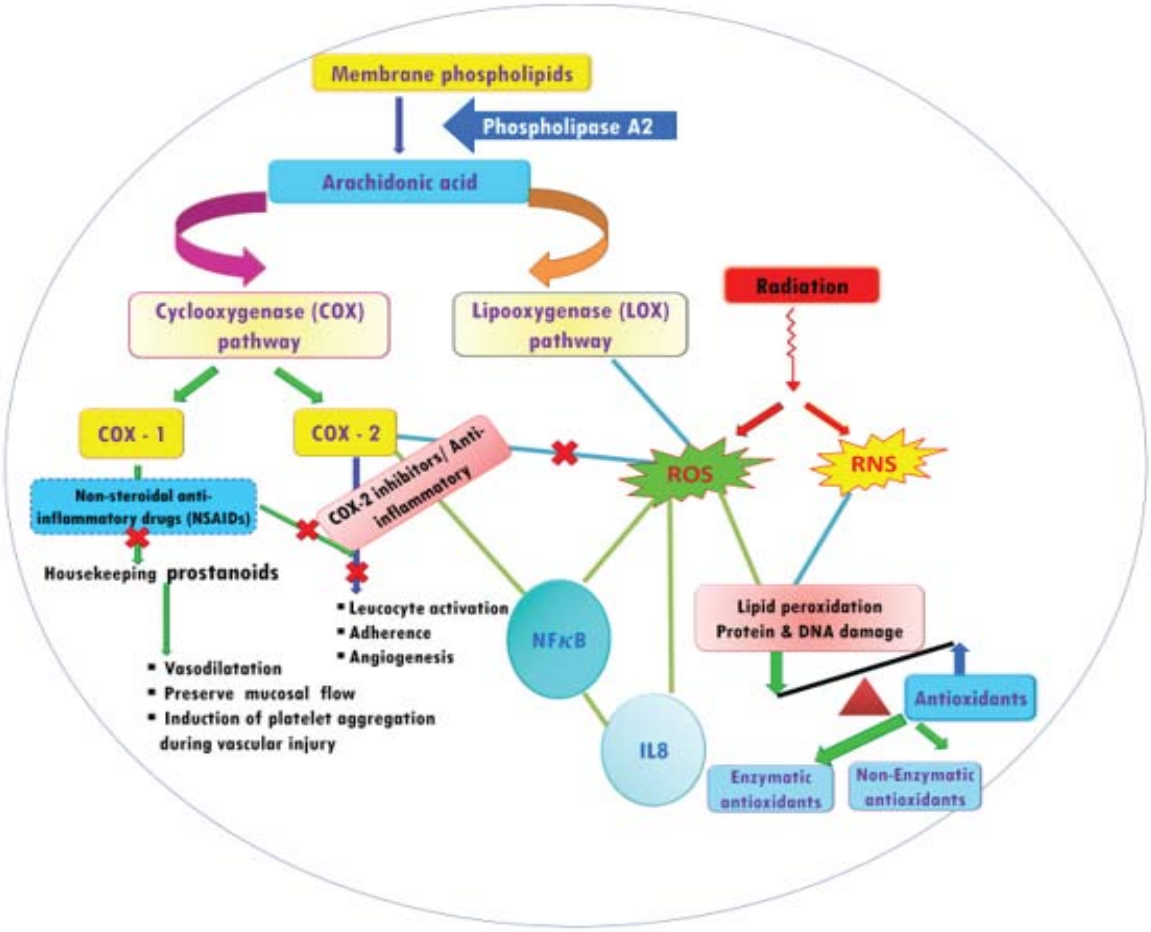

Figure 1. Modus operandi and biochemical relationship of anti-inflammatory and antioxidant agents in targeting radiation induced ROS formation.

ylmethylphenol hydrochloride[35] and crude plant extracts of *Tridax procumbis L.* and *Dioscorea opposite*[36] have also been reported to exert anti-inflammatory, antioxidant, and a variety of other pharmacological activities through inhibition of COX-2 mediated inflammatory responses[37-38]. The hypothesis with respect to the mechanism of action is described in Fig. 1.

6. COMPREHENSIVE DELIVERY SYSTEM FOR FEEDING

During times of high risk of radiation exposure, the person entering such area must ensure to bear the protective coverings in the form of suits, jacket, coat etc. The person who is basically operating in CBRN environment has to be satisfied of hunger and thirst. It becomes crucial to provide the suitable diet which not only takes care of basic nutrition, energy requirement but also enable the body's immunity to boost to fight against the potential threats. It keeps body hydrated and provides enough phytochemicals such as vitamins, antioxidants, and dietary fibers to overcome the detrimental effect of entities generated due to CBRN environment exposure[39]. When the hands are held tight with the arms and ammunitions, the delivery system suitably fabricated/amalgamated with the suit can be very handy and user-friendly approach. The canister/bottle / pouch contains sterile food within must be capable of resisting radiation exposure. It should be preferably a sterilizable and reusable system. The tubing mounting an orifice at one end opens in vicinity to the mouth cavity and can deliver item with a gentle press. The flow-able meal in liquid or semisolid form would be the choice of customer. A variety of menu could be designed and be delivered with above delivery system without introducing monotony in CBRN Meal. At present the design and development of such system is meager in most of developed and developing nations in general[40].

7. PROTECTION OF FOOD

Food may become contaminated from enemy employment of NBC weapons/agents or from terroristic contamination of food procurement facilities and food supplies. The NBC agents may be introduced during production or in the storage area of the procurement facility; while the product is in transit; at the military storage facility; or at the unit food service facility. Regardless of where the agent is used, the effect is the same; personnel will become ill if they consume the contaminated food. To ensure food safety, food must be inspected and monitored from its procurement until it is issued to the consumer. Throughout the channels, all services (Army, Navy, Marine, and Air Force) logistic and food service personnel must take precautions to protect substances from hazardous contamination[39-40].

Designated experts are involved in the detection and monitoring of CBRN contaminated raw and processed food materials inclusive of tinned, canned and packed rations; before use, they must inspect all food suspected of being contaminated with NBC agents. They provide advice on the decontamination of food to unit personnel owning the food, or personnel performing the food decontamination as shown in Fig. 2. Depending on the type of contamination and packaging, the food may be; Consumed without being decontaminated; Decontaminated and then consumed; Destroyed. Some items may be held to allow time for natural decay of nuclear or chemical contamination before consumption. The commander, with advice from veterinary/food safety expert, makes the decision on the disposition of the food[40] as shown in Table 2.

DO's	**Don'ts**
• **Consume only covered food products.** • **Eat canned foods.** • **Consume milk, fruit and vegetables bought or picked before release of toxic material and stored indoors in sealed packaging.** • **Consume peal able fruits and vegetables such as banana, oranges, cabbage, etc.** • **Decontaminate food storage containers thoroughly before opening.**	• **Avoid water from open wells/ponds.** • **Avoid consumption of contaminated crops and vegetables, water or milk.** • **Avoid drinking fresh milk or eating fruits and vegetables grown in the affected area.** • **Avoid consumption of flours stored in jute bags.** • **Avoid dairy and meat products to avoid secondary contamination.**

Figure 2. Dos and Don'ts for food consumption during CBRN scenario.

8. EFFECT OF CBRN AGENTS ON THE QUALITY OF FOOD AND THE DECONTAMINATION PROTOCOLS

The chemical contamination of the processed foods supplied in impermeable containers such as cans, bottles etc. can be resolved by immersing in boiling water/ soap water/ spraying with decontaminating solution-2 (DS2) for 30 minutes followed by rinsing and aeration (Table 2). And if the food is not packed in impermeable material and suspected to be contaminated with chemical agents it must be discarded. For biological decontamination of the packed food supplies the impermeable containers are boiled for 15 min/washed with soap and water followed by immersing in disinfectant solutions such as chlorine, bleaching solution, 5 per cent sodium carbonate, HTH (calcium hypochlorite) solution, super tropical bleach (STB) solution, 2 per cent per acetic acid. and aeration of the containers[41]. For nuclear decontamination the supplies must be washed with soap water followed by rinsing or brushing and wiping the contamination from surface. If the food is exposed the portion infected can be trimmed. The chemical agents such as Mustard, N-Mustards, Arsenicals,

Table 2. Contagion and de-contagion methods[39-42]

Priorities during CBRN scenarios	Avoid contamination- 1- By using barriers 2- Specific entry and exit procedures 3- Preventing secondary contamination to spread	Detection and Decontamination- By specific methods (preferably remote sensing). Rapid methods must be practiced so as to sustain operation. Priorities the food group and packaging material.	
Biological Toxins and microorganisms, biological derived agents	Mostly such contaminations do not change its physical appearance. Packaging material such as flexible films/ metal cans/ glass bottles etc. are highly impermeable for most of the biological threatening agent. Products handled in sealed storage containers such as freezers, refrigerated trucks, or rail cars are safe with respect to biological contamination till these are sealed or not exposed. Packing material is non-nutritive for microorganisms and therefore it would be non-life supportive, hence is self-decontaminating except for spores.	Rapid detection methods are essential to be applied for effective countermeasures at designated facility. Use boiling water/ Soap water for washing, use disinfectant such as bleaching powder, 5% Sodium carbonate solution, 2% per-acetic acid solution etc.	
Chemical	Nerve agents / sulphur mustard, vesicants and arsenicals are most hazards and are either adsorbed or absorbed. In general causes gastrointestinal irritation/ systemic poisoning etc. Phosgene/hydrocyanic acid/ chemical irritants and toxic smokes are main culprit for food contamination not protected suitably. Fatty foods, water rich food such as fresh fruits and veg's having crystalline texture and grainy foods (sugar/ grains) attract deep penetration of nerve agents.	Quick tests kits based on paper strips/ handy colorimeter are extremely helpful for rapid detection and to suitable decide the next course of action in contaminated to sustain the fight. Decontamination is rather challenging but Boil water immersion, spaying disinfectants solution may help up to certain extent.	
Radio nuclear	Direct contamination results when the reagents fallout on food and leads to its surface contamination	Indirect contamination is by eating the contaminated foods	Induced contamination happens when Exposed to sufficient neutron flux
	Washing with disinfectant solution/ Brushing the infected surface/ wiping chlorine/ trimming of contaminated part in case unpacked food		

nerve agents, Phosgene, Cyanogen agents, Irritants, smoke and white phosphorus imparts acidic and bitter taste, discoloration of the natural pigment and objectionable flavour to the foods exposed[42]. Usually the sealed metal cans, airtight glass bottles followed by metal foil laminates, wax papers, multilayer bags, cellophane, card board, wooden crates provide good protection from chemical vapors, and liquid chemical hazards of CBRN Environment, but the paper, canvas and textiles provide no protection to the food. The liquid chemical agents basically show their persistency in varied climatic conditions. They last long in calm sunny, snow bound areas (-10 °C) followed by sunny around (20 °C) with light breeze while wet and heavy wind do not favor their persistency[43].

9. CONCLUSIONS

The future war conditions and patterns are not obvious and the use of chemical, biological, radio-nuclear agent will be in any form may lead to serious detrimental effect on present living being in the area of incident. In such conditions protecting life with suitable life support aids would be an effective step to cope and overcome the current challenges of the war field. At times the food becomes a matter of survival and strength against fighting these situations and provides required source of energy and vital nutrients which can protect or delay the harmful effect of CBRN entities. At DRDO-Defence Food Research Laboratory the processed food are being packed in multilayer flexible packing material subsequently by secondary and tertiary packing material. The laboratory also has experience and expertise in the development of packaging materials for protective packaging of foods during NBC conditions. These materials act as strong barrier however with availability of infrastructure and expertise in various unit process operations which can be used in unison in furtherance of multi-target, combination processing and preservation, focused work for the development of nutrient supplement, its delivery system and packing which can address various challenges present in the CBRN conditions to survive life and to sustain missions is essential for future war scenario.

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ACKNOWLEDGEMENT

The authors are grateful and acknowledge the constructive suggestions, support, and meticulous guidance of Head Grain Science & Technology Division and Head Fruits & Vegetable Technology Division.

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