



DRDO Herbal Technologies: Military and Civil Applications

Rajesh Arora

Introduction

India's military is a human-intensive workforce with nearly 1.3 million defence personnel and over 2.0 million personnel in reserve. In addition, to cater to the nation's security needs – both external and internal – India has over 1.0 million paramilitary personnel. The military personnel are deployed in diverse harsh environmental conditions to guard national sovereignty under diverse geoclimatic conditions and diverse terrains exposing them to unique conditions that are not perhaps encountered anywhere elsewhere on the globe. Homeland security is an important component of national security. The paramilitary and military personnel inevitably have to participate in low-intensity conflict (LIC) theatres also. Besides, the Indian military has always risen to the occasion and helped in disaster management, whenever there has been a natural calamity. The Indian military personnel have also been an integral part of several successful UN peacekeeping missions.

Keeping the physical and mental health of soldiers is paramount from an operational perspective. In addition, they need to be updated and trained to be able to utilize state-of-the-art technologies. They need to be ever vigilant, be prepared for handling any situation and protecting national interests in a rapidly changing world. In order to keep the military fighting fit for operations, there is a need to equip the soldiers with state-of-the-art technologies, often disruptive technologies, products, processes and requisite paraphernalia with a human engineering perspective to support them and handle today's VUCA (volatile, uncertain, complex and ambiguous) environment. DRDO well realizes that this can be only accomplished through continuous, concerted R&D with a focus on new technologies and product development, synergizing the private industry sector along with academia. Today's military operations have to be conducted seamlessly, irrespective of environmental stressors

R. Arora (✉)

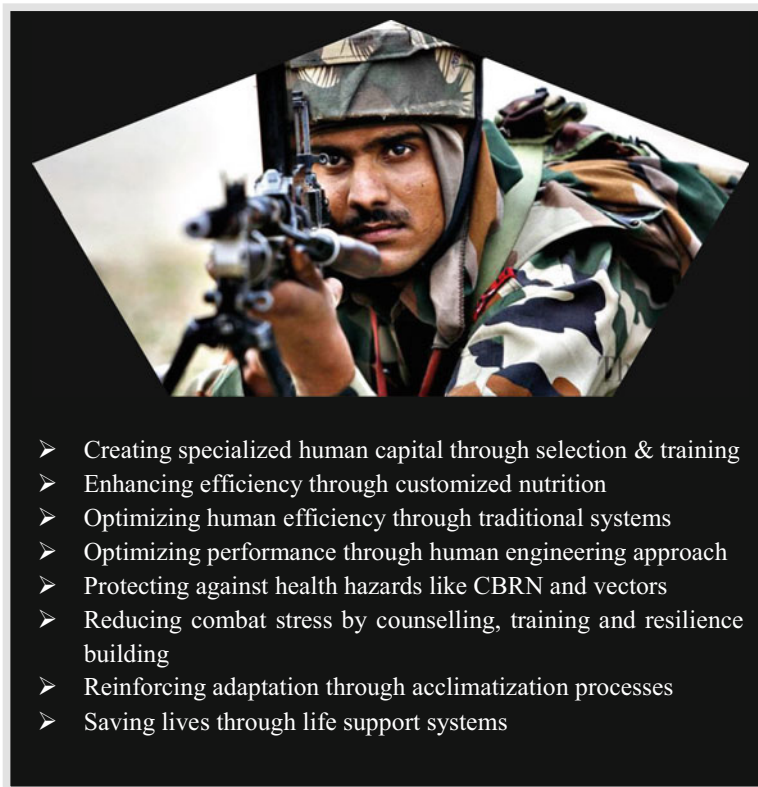
Department of Biochemical Sciences, Defence Institute of Physiology and Allied Sciences,
Defence Research and Development Organization, New Delhi, India

like sub-zero temperatures, torrential rains, snow, extremes of humidity, lashing winds, extreme heat, etc. and/or in a nuclear, biological and chemical (NBC) environment. In the Indian military context, the environmental hazards posed due to the geographical locale often prove more lethal to the health of a soldier than the military operation itself. More than the threat from enemy bullets is the threat of fluid loss from the body under desert conditions or frostbite and high-altitude pulmonary oedema on mountaintops in winter. High pressure of the water column can limit the performance of submariners. Even those who escape sickness may face problems of performance at altitudes in the Eastern and Western Himalayas, where the atmosphere is rarefied due to low oxygen availability. In fact in Siachen sector, more lives have been lost due to the environmental conditions rather than military operations in this ruthless sector.

During the combat active period, the Indian military personnel are exposed to almost all of the environmental and occupational hazards in a single lifetime. The military personnel, depending on their field of activity, are exposed to various stresses in micro-environments like engine rooms of ships, submarines, aircraft cockpits, crew compartments of tanks and other combat vehicles which are usually cramped, hot, polluted by noise, smoke and toxic gases and radiation, and hence these also pose real threats to efficient performance and health of the warfighter.

The operational needs of the Indian Defence Forces necessitate operations under unforgiving and inhospitable environments, which can severely impact both physical and cognitive performance of the personnel. The Life Sciences laboratories of DRDO are engaged in R&D with the aim to develop processes, products and technologies and effective strategies to protect and enhance the operational efficiency of the Indian Armed Forces. The mandate of the Life Sciences laboratories in Defence Research and Development Organisation (DRDO) is to optimize performance of the of the human-intensive combat force, create soldier-system fit in the various weapon development programmes and help them in meeting the unique operational requirements in conventional and nonconventional warfare situations. The R&D activities of the laboratories are focussed on recruitment, selection and development of appropriate human capital, development of intricate life support systems and technologies to protect against extreme and toxic/lethal environments, promotion of health and well-being of warfighter and development of strategic support systems. The fields of research encompass protective equipments and clothing, physiological-psychological aspects, protection against nuclear, biological and chemical (NBC) warfare and high-altitude agro-animal technologies to meet fresh food requirement of troops at high altitudes, exploiting bioenergy as emergency fuel and meeting instant food requirements for high-altitude battlefield operations.

Over the last five decades, the endeavours of the Life Sciences cluster of laboratories have resulted in:



The Life Sciences group of laboratories of DRDO have made significant contributions towards improving the health and performance of soldiers deployed at high altitude, cold, desert, under water, both in air and space and low-intensity conflict areas. The various labs have also made immense progress in agriculture and food technology for adverse environments such as extreme altitude, space, etc. Further, these labs are also engaged in the development of novel technologies to detect, decontaminate and protect against chemical, biological, radiological and nuclear (CBRN) threats. Research in the various laboratories and sponsored projects cover an entire gamut of areas ranging from biomedical, food and high-altitude agro-animal and bioenergy research. Development of herbal technologies is an important area of research where attention is being focused in DRDO, in keeping with prevalence of rich traditions of diverse systems of medicine in India that have been tried, tested and proved over a period of thousands of years. Perhaps no other system of medicine has stood the test of time for such a long period.

Resurgence of Interest in Herbal Technologies in India

Affordable, accessible and acceptable healthcare for all sections of society is the need of the hour. Meeting the health needs of population of over seven billion people, majority of which reside in developing/underdeveloped countries where the population just cannot afford costly healthcare, has necessitated the revival of traditional systems of medicine and the development of cost-effective and pragmatic strategies for the masses. Besides, the disease preventive as well as curative aspects of Indian herbal medicine, its safety and efficacy proved over thousands of years, have made it a preferred choice amongst the masses. The Indian system of medicine, Ayurveda, has evolved as a result of years of medical practice with medicinal plants in humans. India is endowed with extremely rich biodiversity and is home to innumerable medicinal and aromatic plant species which have been used extensively to prevent and/or cure diseases. Similarly, other alternative systems of health like Siddha, Unani and Homoeopathy are now officially recognized, and a ministry known as AYUSH – Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy – has been set up. In view of the huge population of India, it is imperative to develop cost-effective and sustainable health solutions for the public at large. Only one particular system of medicine cannot meet the health challenges posed by the burgeoning population. It is the author's firm belief that we have to consider the rich, Indian traditional systems of medicine for both their preventive and therapeutic aspects and utilize them for meeting the health challenges of our country. Besides, treatments for all diseases are not available in the allopathic system of medicine. The undesirable side effects of modern medicines, the mounting costs of conventional hospital-based healthcare and the emergence of lifestyle-related diseases are some of the reasons for the population to consider alternative simpler and cheaper forms of treatment. Effective and holistic treatment for several diseases like cancer, AIDS, emerging and reemerging bacterial, fungal and viral diseases, Alzheimer's, Parkinson's and several emerging and reemerging diseases are still not available in modern systems of medicine leading to more and more patients taking recourse to alternative therapies for improving the quality of life. Table 1 enumerates the reason why recourse to herbal medicine is the natural choice for sustainable, affordable and acceptable healthcare for the population.

DRDO has been working on herbals for the last several decades to solve the problems of the soldiers, who guard the borders. There are several problems for which holistic and pragmatic solutions are just not available. It is in these areas that the DRDO herbal technologies lay emphasis on.

Harnessing Herbal Technologies to Meet Military Challenges: DRDO Endeavours

DRDO has been making concerted efforts towards research and development of herbal products with the aim of providing solutions to the unique problems faced by the Armed Forces. Some areas of research where DRDO is focussing its attention

Table 1 Why herbal medicine is a natural choice

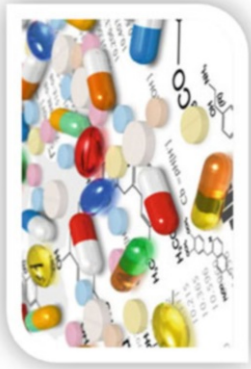
S. No.	Synthetic medicine	Herbal medicine
1.		
2.	Synthetically derived; often nature-imitated or nature-identical	Plants have grown in nature and evolved over millions of years during the course of natural selection
3.	Mostly therapeutic	Both prophylactic and therapeutic; prophylactic action more profound. Herbal medicine focuses on prevention rather than treating a disease or ailment once it arises
4.	Usually acts on a particular biological pathway	Holistic in action; overall wellness
5.	Expensive	Cheaper
6.	Accessible only to section of society, which can afford	Affordable, acceptable and accessible to all sections of society
7.	Few years of animal and human testing	Years (sometimes thousands) of usage in traditional systems of medicine
8.	Requires prescription from medical practitioner	Easier to obtain than prescription medications, mostly available OTC
9.	Limited choice for chronic and acute medical ailments	Possess beneficial, healing properties for the treatment of chronic and acute conditions and various ailments for which treatment is not available in Western systems of medicine
10.	Very few medicines for terminally ill patients	Preferred choice of terminally ill patients
11.	Toxicity/side effects: a major issue	Lesser toxicity/side effects; presence of multiple components countering the toxic action of one compound
12.	Few antiviral drugs	Source of antiviral drugs

Fig. 1 DRDO herbal technologies encompass various areas that touch the lives of the man behind the weapon in multifarious ways in their day-to-day working in difficult terrains and under various operational conditions



vis-à-vis herbal technology development are highlighted in Fig. 1. Documentation of traditional knowledge on herbs of some of the inaccessible areas of the country, mainly high altitude, desert and remote regions of the country, has been carried out. Research to generate scientific data on herbs and their products are under way to explore their potential as antioxidants, immunomodulators, CBRN countermeasures and antistress agents, which would help in improving and protecting the health of troops who are exposed to various occupational and other hazards.

Management of High-Altitude Maladies Encountered by Soldiers

Composite Indian Herbal Preparation

Exposure of living organisms to adverse climatic conditions is known to cause stress, which is a non-specific response to the excess demands imposed on the body. A plethora of stressors like physical, chemical, immunological, biological and emotional factors are involved in the manifestation of stress. Soldiers staying and working in adverse climatic conditions such as cold, heat and high altitude also suffer from stress-induced disorders and at times exhibit decreased or suboptimal levels of physical/cognitive performance due to stress. Adaptogens are biologically active substances that are known to improve physical and mental performance under adverse environmental conditions and induce resistance against stressors,



Fig. 2 Composite Indian herbal preparations: unique adaptogens

e.g. extreme cold and heat, pain and infections. A plethora of herbals possess adaptogenic properties and are used in different traditional systems of medicine for improving overall stress resistance. Taking leads from India's traditional system of medicine – the Ayurveda, a formulation – Composite Indian Herbal Preparation I (CIHP I) has been developed by DIPAS to increase the physical performance of our soldiers who have to operate in high-altitude environments under extremes (Fig. 2). The formulation CIHP I comprises of ingredients (derived from seven different plants used in Ayurveda) and the following aqueous herbal extracts: *Asparagus racemosus* wild roots, 29.23%; *Withania somnifera* Dunal roots, 16.92%; *Pueraria tuberosa* DC tubers, 16.92%; *Mucuna pruriens* DC seeds, 8.46%; *Dioscorea bulbifera* Linn. rhizomes, 8.46%; *Argyrea speciosa* sweet whole plant, 8.46%; *Piper longum* Linn. fruit, 4.32%; and Asphalt extract 7.32%.

CIHP I was tested for its adaptogenic activity using C-H-R animal model. CIHP I helped in improving resistance to C-H-R-induced hypothermia and enhanced post-stress recovery to regain Trec 37 °C. In Border Security Force volunteers, CIHP I intake was found to restrict combat stress-induced deterioration in both physical and mental performance (Srivastava et al. 1996). Another Composite Indian Herbal Preparation II (CIHP II), a combination of numerous plant ingredients and minerals (Table 2), was tested for its adaptogenic action using C-H-R animal model. The acclimatization to hypoxia of extreme altitude was facilitated by the administration of CIHP II during exposure (Grover et al. 1995). Both CIHP I and II augmented oxygen delivery to biological system by increasing red cell 2,3-diphosphoglyceric acid levels during hypobaric hypoxic exposure and improved cellular membrane permeability and maintenance of blood glucose and muscle glycogen levels. CIHPs also regulated the mobilization of lipids from adipose tissue and their preferential utilization for thermogenesis as compared to carbohydrates (Grover et al. 1995; Kumar et al. 1999, 2000). The above studies conducted at DIPAS have indicated that the Ayurvedic herbal preparations/rasayanas with adaptogenic activity increase the high altitude and cold tolerance and relieve the incapacitating effect of stress on operational performance.

Table 2 Composition of CIHP II (460 mg tablet)

Ingredient	Content (mg)	Ingredient	Content (mg)
<i>Withania somnifera</i>	30.0	Abhrak bhasma	10.0
Makardhwaj	10.0	<i>Adhotoda vasica</i>	10.0
<i>Asparagus racemosus</i>	20.0	<i>Argyreia speciosa</i>	10.0
<i>Mandur bhasma</i>	5.0	<i>Carum copticum</i>	05.0
<i>Caesalpinia digyna</i>	10.0	<i>Celastrus paniculatus</i>	05.0
<i>Crocus sativus</i>	5.0	<i>Curcuma longa</i>	05.0
<i>Asparagus adscendens</i>	10.0	<i>Eclipta alba</i>	10.0
<i>Tamarix gallica</i>	3.2	<i>Elettaria cardamomum</i>	05.0
<i>Achillea millefolium</i>	3.2	<i>Eugenia caryophyllata</i>	05.0
Amber	2.0	<i>Exts. Berberis aristata</i>	10.0
<i>Centella asiatica</i>	20.0	Jasad bhasma	05.0
<i>Glycyrrhiza glabra</i>	20.0	Loh bhasma	05.0
<i>Terminalia arjuna</i>	6.4	Mace	10.0
<i>Cichorium intybus</i>	13.8	<i>Mucuna pruriens</i>	10.0
<i>Solanum nigrum</i>	6.4	<i>Myristica fragrans</i>	10.0
<i>Cassia occidentalis</i>	3.2	<i>Piper longum</i>	10.0
Chyavanprash concentrate	100.0	Shilajeet (purified)	20.0
<i>Exts. Capparis spinosa</i>	13.8	<i>Terminalia chebula</i>	15.0

Processed in: *Allium cepa*, *Allium sativum*, *Asparagus racemosus*, *Berberis aristata*, *Boerhavia diffusa*, *Eclipta alba*, *Phyllanthus emblica*, *Phyllanthus niruri*, *Raphanus sativus*, *Terminalia chebula*, *Tinospora cordifolia*, *Tribulus terrestris*

Herbal Antistress Adaptogen: DIP-91

Stress is a part and parcel of modern-day life. Prolonged and persistent stress can lead to psychophysiological and metabolic disorders like hypertension, diabetes, gastric ulcer, cardiovascular ailments, etc. A non-specific, antistress procedure/process and herbal or chemical intervention can help in the restoration of normal homeostasis of the body. The soldier faces innumerable stresses while on military assignments. A potent herbal antistress adaptogen (DIP-91) has been developed for soldiers using a single herbal component, which is specifically effective in alleviating high-altitude stress (Fig. 3).

DIP-91 has numerous benefits: (i) it acts as an anxiolytic, promotes endurance and is a potent rejuvenator/revitalizer; (ii) doesn't alter metabolism during the resting phase; (iii) exerts adaptogenic effect only under conditions of threat to the system; (iv) possesses exceptional antioxidant potential and thereby alleviates oxidative stress; (v) possesses non-cumulative potent adaptogenic activity; (vi) is better than available products in the market (polyherbal/multicomponent preparations; and (vii) is cost-effective, non-toxic, safe and free of heavy metal-associated toxicity.

DIP-91 is very effective as a health food supplement/nutraceutical. It is useful for overall health and well-being under stressful situations as it improves stamina and



Fig. 3 The herbal antistress adaptogen – DIP-91– is useful in high-altitude regions



Fig. 4 *Hippophae salicifolia*: potential application in high-altitude stress management

immunity and helps in adapting to adverse environmental conditions. DIP-91 has been reported to be a potent antistress agent for management of day-to-day stresses faced by the soldier during operations.

***Hippophae* spp. for High-Altitude Stress Management**

The high-altitude medicinal plant species, viz. *Hippophae salicifolia* and *Hippophae rhamnoides turkestanica*, are widely distributed in the Himalayan region and possess adaptogenic properties, which alleviate high-altitude stress. *Hippophae salicifolia* has been shown to have potential application in high-altitude stress management (Fig. 4). Rathor et al. (2015) evaluated the mechanism of action of both the species against multiple stresses [cold-hypoxia-restraint (C-H-R)]. They reported the adaptogenic activity of *Hippophae salicifolia* in facilitating tolerance to CHR in rats. Pretreatment with *Hippophae salicifolia* significantly attenuated reactive oxygen species production, protein oxidation and lipid peroxidation and also helped maintain antioxidant status. Pretreatment of *Hippophae salicifolia* resulted in decreased protein oxidation, and protein homeostasis was sustained by regulation of heat shock proteins (HSP70 and HSP60). Interestingly, heme oxygenase-1, vascular endothelial growth factor and nitric oxide level were also

increased in *Hippophae salicifolia* pretreated rats proving its adaptogenic activity against cold-hypoxia-restraint. Conclusively, aqueous extract of *Hippophae salicifolia* could be used as an adaptogen for high-altitude-associated multiple stress.

Sharma et al. (2015) have attributed the potent in vitro antioxidant potential of the extracts of the leaves of *Hippophae salicifolia* and *Hippophae rhamnoides mongolica* (as compared to *Hippophae rhamnoides turkestanica*) to the in vivo adaptogenic performance in animals during cold and hypoxia exposure under restraint stress. For adaptogenic studies, rats with oral drug supplementation were exposed to cold-hypoxia-restraint (C-H-R) stresses-induced hypothermia to determine endurance. Aqueous extracts of *Hippophae salicifolia* showed maximum (99%) resistance compared to the other *Hippophae* spp. The levels of biochemical parameters such as reactive oxygen species, malondialdehyde, lactate dehydrogenase, superoxide dismutase, glutathione and catalase in blood samples also revealed that the aqueous leaf extract of *Hippophae salicifolia* exhibited superior antioxidant and adaptogenic potential and established its usefulness for high-altitude stress management.

Sea Buckthorn Soft Gel Capsule for Better Acclimatization

With a view to developing prophylactics for soldiers who operate in high-altitude regions, supercritical fluid extracted sea buckthorn seed oil-based soft gel capsules has been formulated by the Defence Institute of High Altitude Research (DIHAR), Leh (J&K). The formulation is extremely rich in unsaturated fatty acids (omega 3,6,9), vitamin 'E' and carotene and contains minerals that confer it with significant antioxidant activity. The high antioxidant activities possessed by the product make it promising for use as a prophylactic for the management of high-altitude maladies (Fig. 5). The formulation improves heart function and blood circulation and increases myelination of neurons, thereby improving cognitive faculties.



Fig. 5 Sea buckthorn seed oil-based soft gel capsule helps in better acclimatization at high altitudes

Herbal Adaptogenic Appetizer for Appetite Modulation

Research has shown that at high altitudes, there is significant weight loss, which is attributable to decreased energy consumption mainly due to lack of appetite. A nutraceutical herbal adaptogenic appetizer has been formulated using spray-dried powder of sea buckthorn and apricot pulp along with the extract of *Rhodiola*, the indigenous medicinal plants of high-altitude Himalayas with exceptionally rich nutritional and pharmacological potential (Fig. 6). The main ingredients include *Hippophae rhamnoides*, *Prunus armeniaca* and *Rhodiola imbricata*. It is rich in flavonoids, polyphenols, sterols, vitamin C, vitamin E, riboflavin, niacin, isorhamnetin, rosavin and carotene. The formulation improves digestion and appetite and augments serum antioxidants.

Protection Against UV Radiation

The military units deployed at high-altitude regions face challenges posed by the harsh environment. The excessive ultraviolet radiation at high-altitude regions, together with hypoxia, cold, wind, dryness and solar radiation, adversely impacts the performance of troops. Providing health service support to the Armed Forces is the key mandate of DRDO. A herbal formulation has been developed that acts as a prophylactic for low humidity and UV-mediated skin damage at high altitude (Fig. 7).

The UV protective cream has anti-photoageing and anti-blemish properties. The formulation contains *Hippophae rhamnoides* (sea buckthorn) seed oil as the major ingredient. The formulation also contains uvinul t 150-ethyl hexyl triazone, uvinul mc 80-ethylhexyl methoxy cinnamate, tinisorb m-methylene bis-benzotriazolyl tetra methylbutyl phenol, uvinul a-diethyl amino hydroxyl benzoyl tetra methylbutylphenol, tinisorb-bis-ethylhexyloxyphenol methoxyphenyl triazine, petroleum jelly, isopropyl myristate (IPM) and other compounds. The formulation



Fig. 6 Herbal adaptogenic appetizer

Fig. 7 UV protective anti-blemishes cream developed by DRDO for use in high-altitude region by the troops



does not contain zinc and has UV protective efficacy equivalent to SPF > 45 along with anti-blemishes and skin-healing properties. The topical formulation can be effectively used as a prophylactic for low humidity and UV-mediated skin damage caused at high altitude.

Another high-altitude herbal UV screen “Umbriel” has been specifically developed to protect the subjects from damage caused by the UV flux prevalent at high altitudes. Umbriel (a registered trademark of DRDO) is a unique combination of herbal agents developed by INMAS, DRDO. It is non-toxic, prophylactic, dermal ointment which has been scientifically tested to cut off more than 90% UV rays, prevent DNA damage, regulate melanin content in the skin, prevent immunosuppression, and counter oxidative stress and photosensitivity. This product has passed highly sensitive tests such as infrared thermography. This innovation is useful for people living in high-altitude regions, tourists visiting high-altitude areas and sportsmen participating in snow/winter games at high altitudes and people who migrate from plains to high altitudes and are unacclimatized to the extreme UV radiations prevalent at high altitudes.

Ensuring Survival in Land Locked Regions During Military Exigencies

The concept of survival garden has been developed by DRDO to meet the health and survival needs of the Armed Forces in case of exigencies arising locally during operations. The ethnic medicinal plant resource especially in the North West, Central and North East Himalayan region are being harnessed for this purpose.

The purpose of survival garden is that the soldiers should be able to utilize the locally available indigenous medicinal and aromatic plants can be utilized for treating common ailments and survival during operational conditions in diverse terrain (Fig. 8). India is extremely rich in phytobiodiversity in view of the prevailing



Fig. 8 The survival garden for soldiers can be immensely helpful during emergency situations

divergent ecosystems and considerable altitudinal variations in the country. The Himalayan ranges possess huge phytobiodiversity in terms of various plant species, including angiosperms, gymnosperms, pteridophytes, bryophytes, lichens, bacteria and fungi. Of this diversity, nearly 25% species are endemic to the Himalayas. The Himalayas are considered to be a treasure house of medicinal, aromatic, edible wild and other important plants, which have been used by the local populations for meeting their daily necessities since ages, and this long dependence on plant wealth enriched their knowledge about the multifarious uses of phytodiversity. The high-altitude regions of Ladakh and Lahaul-Spiti in the North West and Tawang in the North East are strategically important because of the international borders with China and Pakistan. The Armed Forces, deployed in these regions, have to face extreme environmental conditions, as the region is prone to landslides, heavy rainfall, cloud bursts, avalanches and natural calamities. At times, these landlocked areas become inaccessible by road and/or air. In view of the likelihood of availability of food and medicines in such areas becoming compromised under certain operational conditions, a need was felt to develop databases on wild plants that can help sustenance and survival of troops in such regions in case of an emergency. The survival garden can play an important role in helping the troops operate unhindered under any circumstances.

Improving Combat Performance and Operational Efficiency

DIP-G-FIT: A Unique Formulation for Improved Soldier Performance

An oriental fungus that has been used for promoting health and longevity in the Himalayan tracts of India, China, Japan and several other Asian countries has been used to develop a medicinal formulation - DIP-G-Fit for enhancing performance in soldiers (Fig. 9). The fungus grows at high elevations in the Himalayas and has been recognized as a very powerful medicinal mushroom for several hundred years. It is widely used due to its numerous pharmacological properties including antistress, antifatigue, immunomodulatory, health-promoting and longevity-enhancing properties, etc. and is quite popularly accepted as a dietary supplement in Western countries. In preclinical studies conducted at DIPAS, supplementation of DIP-G-Fit enhanced exhaustion time in experimental animals significantly both under



Fig. 9 Performance enhancing DIP-G-Fit formulation

normoxic and hypoxic conditions. DIP-G-Fit can be extremely useful for enhancing performance of soldiers posted at high altitude and improving endurance in sports personnel.

***Cordyceps* Capsules for Improved Physical Function**

Cordyceps sinensis is a high-value medicinal fungus growing on caterpillar in Himalayan region (11,000–14,000 ft), locally known as Kira Ghas or Yarsha Gamboo. The extract of the fungus is effective against hypertension, diabetes, pneumonia, leukaemia, cirrhosis, impotence, tuberculosis, insomnia, joint pain, cough, hypoxia, arthritis, erythropoiesis and chronic bronchitis. Laboratory cultures for the fungus have been established and can serve as a stable source for obtaining its extract, removing the dependence on harvesting from the natural environment.

Cordyceps improves the respiratory function and can be used for treating chronic bronchitis and asthma; improves the functioning of the heart and is helpful in heart rhythm disturbances, cardiac arrhythmias and chronic heart failure; alleviated LDL cholesterol and increases HDL cholesterol; possesses antitumour properties; improves immune system function by modulating the activity of different cytokines like NK cells, ILs and IFNs and protects against free radical-induced damage; improves stamina by increasing ATP synthesis, reduces fatigue; and improves physical function. A formulation developed from *Cordyceps* has been developed, which improves physical function of soldiers (Fig. 10).

Herbal Performance Enhancer

A herbal adaptogenic performance enhancer performer has been formulated using different plant parts, viz. root, leaves, fruits, etc., of high-altitude medicinal plants and exotic plants based on ethnobotanical information (Fig. 11). The herbal formulation enhances physical and mental performance and can be used as a herbal prophylactic for high altitude and as a dietary supplement. The main constituents are *Codonopsis pilosula*, *Astragalus membranaceus*, *P. cocos*, *Rhodiola imbricata*, *Aloe vera*, *Zingiber officinale*, *Ginkgo biloba*, *Bacopa monnieri*, *Withania somnifera*



Fig. 10 *Cordyceps* for improved physical function of soldiers

Fig. 11 Perfomax: a herbal adaptogenic performance enhancer



and *Tribulus terrestris*. The formulation is rich in vitamins A, B series, C, D, E and GSH, besides astragalosides, choline, beta-sitosterols, pachymaic acid, withanine, protodioscin, triterpenes, ginkgolides, anthraquinones, aloin, shogaol, gingerol and bacosides. The herbal prophylactic is useful for high-altitude problems and as a dietary supplement.

Antistress Multivitamin Sea Buckthorn-Based Herbal Beverage

A multivitamin herbal beverage has been developed by the Defence Institute of High Altitude Research (DIHAR), Leh, from the fruits of the plant *Hippophae rhamnoides* that grows wild in the mountains (Fig. 12). The lab has developed the technology for processing of fruits of sea buckthorn (*Hippophae rhamnoides*) with high retention of bioactive compounds. This tasty drink is rich in vitamin A, B1, B2, C, E and K, carotenoids, flavonoids and phytosterols. The drink is being supplied to the Army for the troops located in the Siachen area. The beverage is very popular amongst the troops not only because of its rich vitamin content but also because it does not freeze even at sub-zero temperatures and, furthermore, possesses antistress properties.



Fig. 12 Multivitamin sea buckthorn-based herbal beverage developed by DRDO has proved useful for the soldiers operating in the Siachen sector

DRDO Herbal Tea for Alertness and Efficiency

Oxidative stress has been implicated in the development of several degenerative diseases. Utilizing ethnobotanical leads from the locals residing in the high-altitude region, Defence Institute of High Altitude Research (DIHAR), Leh, has formulated an antioxidant-enriched herbal health tea based on indigenous high-altitude medicinal plants of the Ladakh Himalayas (Fig. 13).

The product is a combination of high-altitude herbal plants having a high antioxidant content. Sea buckthorn (*Hippophae rhamnoides* var. *turkestanica*), salam panja (*Dactylorhiza hatagirea*), local tea (*Bidens pilosa*), local caraway (*Carum carvi*), black caraway (*Bunium persicum*), oregano (*Origanum vulgare*), local mint (*Mentha longifolia*), yarrow (*Achillea* sp.), rose root (*Rhodiola* sp.), etc. are the key ingredients of this herbal tea formulation. The herbs used in making this herbal tea are widely used since ages in the Tibetan system of medicine (Amchi system) for the treatment of various ailments such as the body ache, cold, cough, fever, gastritis, headache, stress, high-altitude mountain sickness, high blood pressure, indigestion, memory loss and weakness, etc.

Studies in animal models have shown that the herbal tea reduces the onset of oxidative stress. The tea is rich in natural antioxidants like polyphenolic compounds, flavonoids, etc. The herbal tea is invigorating, stimulating and stress relieving, apart from being a thirst quencher.

Pain Management

Pain management often becomes an issue, especially in the cold and low barometric pressure conditions in high-altitude environment for the soldiers. A composite herbal formulation – Joint Care Gel meant for targeted topical application on joints to get relief from joint pain – has been developed by the Defence Institute of High Altitude Research,



Fig. 13 DRDO herbal tea for alertness and efficiency

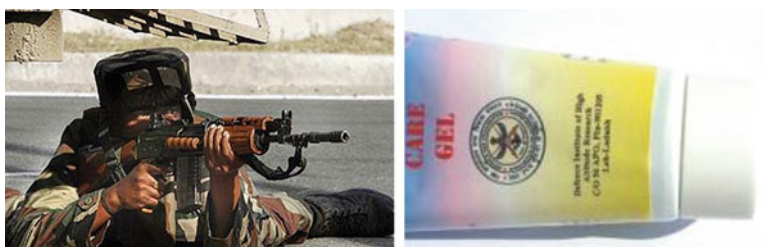


Fig. 14 A herbal formulation for pain management especially in the cold and low barometric pressure conditions (high-altitude environment) for the soldiers

Leh, from essential oil extracted from leaf of winter green, eucalyptus and kernel of apricot mixed at standardized optimal ratio with *Aloe vera* gel base (Fig. 14).

The formulation is rich in methyl salicylate, oleic acid and cineole. The Joint Care Gel can be topically applied in area of pain, by gently rubbing it and covering the area with dry warm cloth for 15 min. It should not be applied on cuts, burns and wounds. The botanical ingredients include *Eucalyptus globulus labillardiere*, *Gaultheria fragrantissima* and *Prunus armeniaca*. The gel is reddish in colour and has a characteristic odour due to the presence of aromatic camphoraceous compounds and has sweet woody smell.

Management of Toothache

Toothache can be a problem anytime, especially when soldiers are on the move and have no access to modern medical care in the remote jungles, desert or mountainous regions. The nearest dental clinic may be several kilometres away. An anti-toothache formulation has been developed incorporating the ingredients of locally available Himalayan medicinal plants, which can come in handy during operations to alleviate



Fig. 15 Amtooth and its use for toothache management by soldiers

toothache in emergencies (Fig. 15). The formulation contains ethanol isolates of five plants and essential oil of two plants.

The product relieves pain within 2 min of application and reduces swelling of gums, and there is no burning sensation on gums. It is also effective in hot and cold sensation of gums (sensitive teeth).

Herbals for Low-Intensity Conflict (LIC) Operations and Crowd Management

Low-intensity conflict entails armed conflict between law enforcement agencies and non-regular armed militias, which could include terrorist groups, guerrilla fighters, rioters, etc. (Chadha 2005). The involvement of the local populace either overtly or covertly is a common feature of most low-intensity conflicts. The low-intensity conflicts usually involve contiguous regions/states and ultimately aim to destabilize and weaken the nation. India has witnessed several low-intensity conflicts of varying nature, degree and contexts, and these pose immense problems to law enforcement agencies in general and the military in particular for handling such issues with a sense of responsibility. Use of force under difficult inevitable circumstances often results in death or maiming of local populations leading to immense furor, e.g. the use of pellet guns to disperse mobs in North India resulted in serious eye injuries to several people. Subsequently, the Supreme Court of India ruled that being a welfare state, it is the duty of the government to ensure safety of its people as well as security forces. With a view to managing LIC operations less fatally, oleoresin-based products like Capsispray™/Capsigrenade™ – an eco-friendly, less-than-lethal weapon, based on oleoresin extract of chilli (Bhut Jolokia, *Capsicum assamicum*) developed by DRDO (Fig. 16) – can come very handy.

Capsi-based products are suitable for the law enforcement agencies, police and paramilitary forces for use in the LIC-affected areas, for riot control and for protection of vital installations from sabotage, crime prevention, flushing out hiding people as well as civilian applications like personal or area protection and self-defence. Capsi-based products can be used as a handheld spray or as a hand grenade or thrown through projectile/launchers as ball or shell or through water cannon as



Fig. 16 *Capsicum assamicum* plant (left) and fruits (right) – the source of oleoresin-based products like Capsispray™/Capsigrenade™ produced by DRDO



Fig. 17 OR-based grenade for crowd management

fine spray. They have no explosive fuse for burning chilli powder and thus do not need any approval from explosive agency.

One of the aims of the civil/military authorities during operations is to catch hold of the miscreants alive and get complete information about their ring leaders. Particularly when they take shelter in hideouts or in house/building, it is very difficult to take them out without collateral casualties. During counterinsurgency operations, security personnel have to disarm/incapacitate agitated individuals, disperse the crowd or capture militants held up in a bunker or building. The available methods in vogue are normally lethal in nature, e.g. small arms and grenades, which result in the loss of life/bodily injuries. There is a need for a non-lethal aerosol chemical-based weapon system, which is instantaneously effective and totally safe in controlling agitated and misguided individuals and can be used to incapacitate them leading to their capture.

In the Defence Research and Development Establishment (DRDE), Gwalior has developed a unique non-lethal munition, named as oleoresin-based grenades (Fig. 17). The product is totally safe, simple to operate, user-friendly and extremely useful for the above purpose. The body of the grenades is made of plastic, which melts when the grenade bursts thus making its throwing back difficult. The grenade



Fig. 18 Capsispray™ is a novel and eco-friendly less-than-lethal chilli spray derived from *Capsicum assamicum* (Bhut Jolokia) oleoresin. Capsispray™ is highly suitable for Indian troops for use in low-intensity conflict areas as well as for riot control, personal protection self-defence and crime prevention, etc.

can be thrown by hand up to 30 m to the hideouts/agitated mob. The grenades when applied emit tear gas for 60–80 s after a delay of 1–2 s, making the person come out due to lachrymation, irritation and suffocation. The product has been inducted into the services and is being used for the riot control agents by services, CAPFs, state police and other paramilitary forces. The product is useful for peacekeeping purposes and combating terrorism. It can be used to incapacitate terrorists and flushing them out from hideouts (tunnels, fields, dense jungles, broken grounds, etc.) without casualties. The grenade can be effectively used for controlling agitated and misguided individuals and can be used to incapacitate them within no time.

Capsispray™ is a unique, eco-friendly less-than-lethal chilli spray developed from Bhut Jolokia (*Capsicum assamicum*) (Fig. 18). It contains Bhut Jolokia oleoresin dissolved in a suitable carrier solvent and pressurized under propellant. Capsispray™ is available in container can (aluminium make) of length 11 cm and diameter 3.5 cm. The water capacity of the container can is 80 ml, net weight is 35 gm, and volume content is 55 ml net. The effective range is up to 20 ft. The spray end of the nozzle should face the desired area of contamination. The nozzle is pressed downwards to discharge spray. The ideal usage pattern is short bursts of 2–3 s to contaminate the area. It is advisable not to store the container above 50 °C temperatures and in areas prone to heating because excessive heating may cause this unit to burst. It causes coughing and skin and eye irritation to exposed person. It incapacitates the person for 20–45 min. Simple ‘lock-unlock’ mechanism is provided for using the product by any responsible person. The salient features of the product include the following: is an effective human/animal deterrent device, has diverse applications (use against individual or mob) and is useful in stationary and mobile systems; safety of usage has been established as the effects are reversible. The product is useful from personal security point of view, for self-defence, crime prevention, mob control, etc.

Ensuring Survival in Extreme Environments

Managing Frostbite Using Herbs

In snowbound areas of the high mountains, one of the major problems encountered is frostbite, which if not treated timely can lead to irreparable tissue damage leading to amputation of the affected parts. DRDO has attempted to develop appropriate prophylactics and curative measures to solve this problem often encountered by soldiers operating at high altitude. Based on extensive research, an *Aloe vera*-based cream has been developed by DRDO for the management of frostbite – the cream is non-greasy and does not cause any sweating or flaking and does not freeze even at low temperature (0 °C). Besides its application for management of cold injuries, this cream can be used for treating burns, wounds, ulcers, cracked and chapped skin and cuts and as an antiseptic dressing.

During trials in the Siachen glacier region, a combination of pentoxifylline, vitamin 'C' and low dose of aspirin along with ALOCAL (*Aloe vera* cream) application in soldiers showing early signs of cold injury was found effective in reducing morbidity (Fig. 19). Topical application of *Aloe vera* cream (50%) prophylactically along with tab aspirin 150 mg once daily, tab pentoxifylline 400 mg and tab vit C 500 mg three times daily and rewarming in decoction of tea leaves as therapy has been proved to be an effective remedy in preventing and ameliorating cold injuries in high altitude. The limbs of several soldiers were saved from amputation as a result of the use of this formulation in the cold, ruthless Siachen glacier sector.

Managing Difficult to Heal Wounds

Wound healing is classically divided into haemostasis, inflammation, proliferation, and remodelling. Abnormalities arising due to wound per se and during the wound repair process cause a great deal of physical and mental ordeal to patients. A unique herbal formulation, viz. Herbo Healer for management of normal as well as chronic, non-healing wounds, has been developed from a single constituent of herbal origin by the Defence Institute of Physiology and Allied Sciences (DIPAS) – a constituent laboratory of DRDO (Fig. 20). It promotes rapid and aesthetic healing, is rich in natural antioxidants and bioactive polyphenols/flavonoids and aids in healing of wounds by acting at cellular and molecular level. It has been proven to augment healing via wound contraction, re-epithelialization, cellular proliferation, collagen accumulation and neovascularization. Herbo Healer has antibacterial properties and has been shown to be way better than silver sulfadiazine and other iodine-based ointments. The safety and toxicological studies have proven it to be safe for dermal applications. ToT has been transferred to reputed firms.



Fig. 19 ALOCAL (an *Aloe vera*-based cream developed by DRDO) application in soldiers exhibiting early signs of cold injury has been found to be very effective in reducing morbidity in glacier region

Fig. 20 Herbo Healer is an effective wound healer and promotes scar-free healing



Prevention Against Snakebites

Snakebites are common in jungles and pose environmental hazard that is associated with significant morbidity and mortality, if the snake is poisonous and the individual is not timely treated with anti-snake venom (Singh et al. 2008). The soldiers have to operate in jungles, where wildlife is in plenty. For the military, it is definitely an occupational hazard. The best method to reduce human-snake encounters is to be cautious and avoid them; however, this is not always possible in snake-infested areas, and snake repellents can be quite useful in such scenarios. Murdock et al. (1990) and Krysa-clark et al. (2004) have highlighted the importance of prevention and emergency field management of venomous snakebites during military exercises.

Defence Research Laboratory (DRL), Tezpur, has developed a snake repellent formulation, which is effective against deadly poisonous snakes including spectacled cobra (*Naja naja*), banded krait (*Bungarus fasciatus*), monocled cobra (*Naja kaouthia*), saw-scaled viper (*Echis carinatus*) and Russell's viper (*Daboia russelii*) (Fig. 21). The formulation is eco-friendly; it does not harm the snake, it only repels the snake so that it goes away from the area where the formulation has been used. The formulation is available in liquid and granular form; it can be used in gardens and home also. The formulation is of herbal origin and has a shelf life of 1 year under any environment conditions. Ethnic herbs, mainly from eastern India, have been used to develop the formulation. The formulation is non-toxic, non-hazardous and non-mutagenic and contains no phenolic compounds. The formulation has been found to be effective in warding off snakes from Army units, installations and residential areas in the North East region.

Herbals for Alleviating Seasickness

Seasickness is a form of motion sickness; it is hardly fatal, but symptoms such as nausea, stomach cramps and vomiting caused can be quite debilitating, affecting performance of the seafarers. In critical military operations, seasickness can impede mission accomplishment. The Indian Navy had reported that the Somalian pirates use a plant called khat (*Catha edulis*) for alleviating symptoms of seasickness and improving performance. *Catha edulis* is native to the [Horn of Africa](#) and the [Arabian](#)



Fig. 21 The snake repellent formulation developed by the Defence Research Laboratory (DRL), Tezpur, is effective in warding off snakes from Army units, installations and residential areas of the North East

Peninsula, where khat chewing is a social custom dating back thousands of years. *Catha* (khat) contains a monoamine alkaloid – cathinone (an amphetamine-like stimulant), which causes excitement, appetite loss and euphoria. The World Health Organization (WHO) classified it as a drug of abuse in 1980 as it can induce psychological dependence. Based on the information provided, khat was evaluated for its ability to reduce conditioned taste aversion in rats (a model system for motion-induced nausea and vomiting) and compared to some Indian medicinal plants. IBG-15 was found to be more effective and safe in alleviating CTA as compared to *Catha edulis* (Fig. 22).

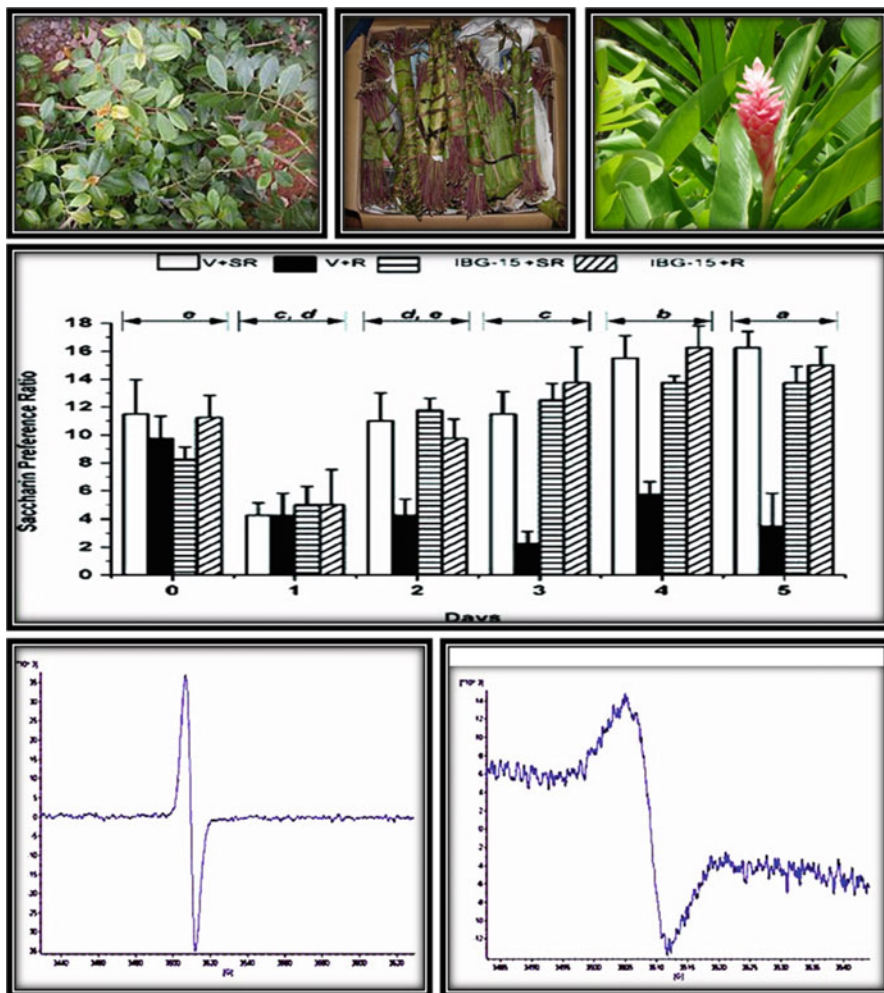


Fig. 22 Evaluation of some medicinal plants for alleviation of seasickness utilizing conditioned taste aversion (CTA) as a model system

Mitigating CBRN Hazards

One of the major threats faced by the Armed Forces is attack by CBRN agents. Very few medical countermeasures are available in the armamentarium of the services to deal with such hazards, which is life threatening in nature. DRDO labs are engaged in R&D on developing safe and effective CBRN countermeasures from herbals, and several leads have been obtained. Some such leads obtained vis-à-vis CBRN countermeasures are discussed in the ensuing sections.

Radiological/Nuclear Countermeasures

Attempts have been made by various researchers to classify radioprotectors into different categories. However, there is no universal classification that is unanimously acceptable. A radioprotector can be defined as a substance [element, chemical or a compound of synthetic or molecular nature or biological compound(s)] that reduces the deleterious effects of radiation, when administered to living organisms, usually prior to irradiation (prophylactic administration), while radiorecovery agents are those that help in recuperation and augment recovery once the living organism has been exposed to radiation. Most agents available today fall in the former category. Since the damage resulting due to ionizing radiation in most cases cannot be totally reversed, the currently available radiorecovery agents exhibit limited efficacy. There is immense interest now to develop both categories of agents so that radiation damage can be treated holistically.

Vasin (1999) of the Institute of Aviation and Space Medicine, Moscow, classified prophylactic antiradiation drugs into the following categories: (i) drugs having short-term and long-term action drugs, (ii) drugs that stimulate radioresistance, (iii) drugs that suppress symptoms of primary radiation reaction, (iv) drugs that detoxify early and (v) drugs that act by absorption or elimination of radionuclides from an organism. Nair et al. (2001) have classified radioprotective agents into three categories: (i) radioprotectors, (ii) adaptogens and (iii) absorbents. Radioprotectors include compounds like antioxidants and others that possess sulfhydryl groups. Adaptogens in general are non-toxic stimulators of radioresistance. Usually these are natural biological protectors that offer protection against low levels of ionizing radiation primarily by regulating immunity and modulating the endogenous antioxidants, thereby improving non-specific resistance in biological systems. The last category comprises of absorbents that protect against internal radiation injuries that result due to ingestion of radionuclides. Such agents prevent the incorporation and absorption of radionuclides like ^{90}Sr , ^{137}Cs , ^{239}Pu , ^{131}I , etc. A large number of plant-derived compounds are known to possess highly effective absorbent capability.

The High-Altitude Himalayan Plant Species as Radiation Countermeasure Agents (Fig. 23)



Fig. 23 The high-altitude medicinal plants from the Himalayan region were evaluated and have shown immense potential as radiation countermeasure agents

Podophyllum hexandrum Royle

Podophyllum hexandrum is a medicinal plant species of the Himalayas listed as an endangered species. It is the natural source of podophyllotoxin and other aryltetralin lignans and several other bioactive constituents. In modern systems of medicine, podophyllotoxin finds use as a precursor for the semi-synthetic anticancer drugs etoposide, teniposide and etopophos and other antiarthritic drugs. These drugs and other derivatives, based on podophyllotoxin, find use for the treatment of leukaemia, Kaposi's sarcoma, lung and testicular cancers, dermatological disorders like warts, rheumatoid arthritis, psoriasis, malaria, etc. In ancient Indian traditional system of medicine, *Ayurveda* plant has been mentioned as 'Aindri' – a divine drug in ancient literature (Singh and Shah 1994). *Podophyllum hexandrum* has been used as a cure for allergic and inflammatory conditions of the skin; biliary fever; burning sensation; cold; constipation; cancer of the brain, bladder and lung; erysipelas; Hodgkin's disease; insect bites; mental disorders; monocytoid leukaemia; non-Hodgkin's lymphoma; rheumatism; septic wounds plague; and venereal warts since ages (Chatterjee and Pakrashi 1996).

The radioprotective properties of *Podophyllum hexandrum* have been evaluated in detail at INMAS. The plant *Podophyllum* belongs to the family Berberidaceae and is commonly known as: Bankakri, Papra, Himalayan mayapple, Banwangam and Venival Patvel. *Podophyllum hexandrum* is found at altitudes above >2500 m, in the Himalayan ranges of India, including Sikkim, Jammu and Kashmir, Himachal Pradesh and Uttaranchal. Two other species, viz. *Podophyllum montanum* and *Podophyllum peltatum*, are found in Western China and North America, respectively. The plant contains picropodophyllotoxin, podophyllotoxin, epipodophyllotoxin, podophyllotoxin- β -D-

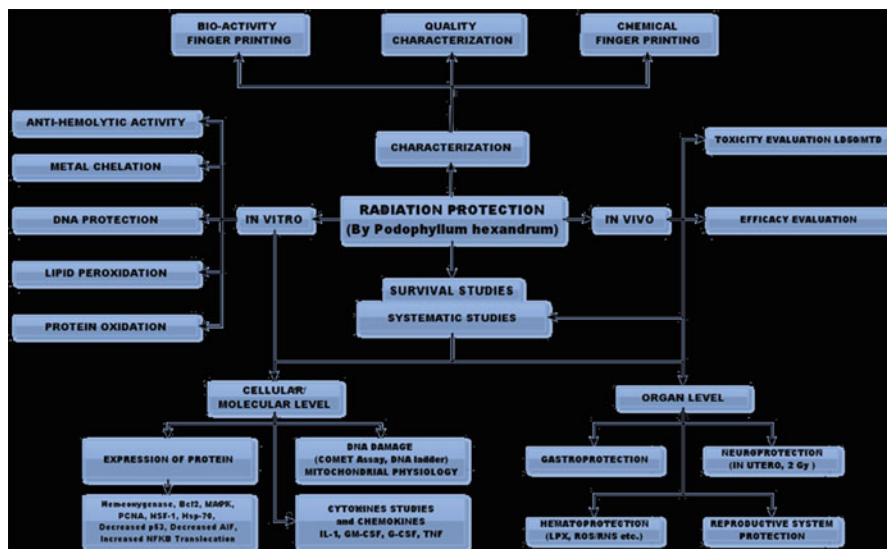


Fig. 24 The multifaceted mode of action of *P. hexandrum* has been elucidated via experimental studies

galactopyranoside, 4'-demethyl podophyllotoxin, quercetin-3-O- β -D-galactopyranoside, kaempferol-3-O-glucoside, deoxypodophyllotoxin and podophyllin.

Radiation is one of the most lethal sources that is capable of inducing severe state of oxidative stress in living systems causing mortality in mammals. In a 30-day survival study using strain 'A' Swiss Albino mice, our group showed that the crude extract of *Podophyllum hexandrum* possesses the ability to save more than 80% animals with administration of a single dose 2 h prior to 10 Gy exposure (Goel et al. 1998, 2000a, b; Arora et al. 2005d). Subsequent studies established that using *Podophyllum hexandrum* extract, a dose reduction factor (DRF; LD₅₀: treated group/untreated group) of 1.33 was achievable. In order to unravel the mode of action, the radiation-induced multi-organ dysfunction needs to be investigated at different levels of hierarchy of organization, and, therefore, our group investigated the organ-level protection rendered by *P. hexandrum* in greater detail (Fig. 24). *Podophyllum* has been shown to protect various organs and systems, including the haemopoietic system, gastrointestinal system, reproductive system and central nervous system (Arora et al. 2005a,b,c, 2006, 2007a,b, 2008a,b,c, 2009, 2010a,b,c,d,e, f,g, 2011a,b; Gupta et al. 2008), (Arora et al. 2010a,b,c,d,e,f,g; Singh et al. 2009a, b; Sagar et al. 2006; Chawla et al. 2005a, b, 2006; Gupta et al. 2003, 2004; Yashavardhan et al. 2016).

Studies by our group have shown that one of the mechanisms by which *Podophyllum hexandrum* renders radioprotection is modulation of radiation-induced oxidative stress. Podophyllotoxin and other aryltetralin lignans in combination with rutin have been shown to play a crucial role in radioprotection. Whole-body radioprotection by *P. hexandrum* is now well established (Fig. 25).

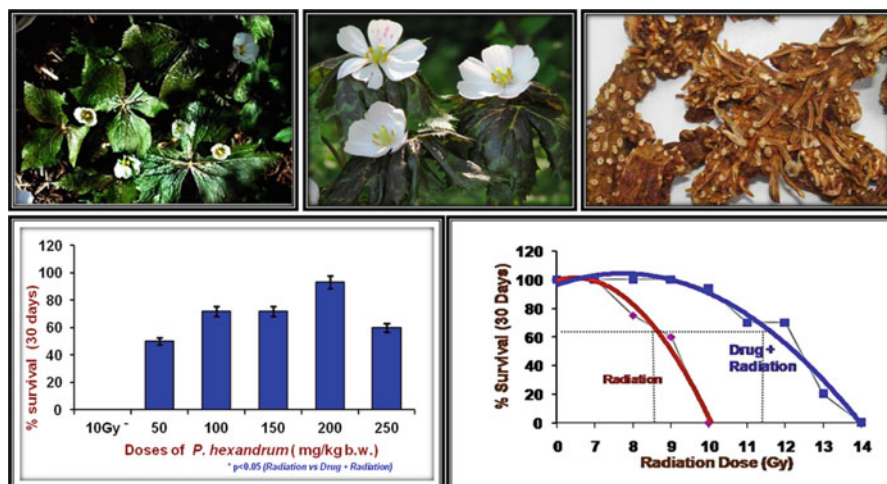


Fig. 25 Plants and rhizome of *Podophyllum hexandrum* (Himalayan mayapple) yield compounds that act as effective radiation countermeasures

Hippophae rhamnoides L.

Hippophae rhamnoides L. belongs to the family Elaeagnaceae and is commonly known as sea buckthorn or chuma, Ames, dhurchuk or milech and tarru. The plant is a spiny shrub or small tree, with a height between 2–4 m, and berries are fleshy and an important source of antioxidants. The plant is hard, drought and usually cold-tolerant plant, and shoots are modified into spines. The leaves are lanceolate – linear, obtuse and with peltate and stellate scales on lower surface. Male flowers are clustered at the base of shoot; petals free suborbicular, while female flowers are pedicellate inclusions (2–4), petals: 3–4 mm long, united utricles subglobose, succulent, red and orange coloured. Seeds are solitary, unequally bilobed, light, black and very hard. The plant is widely distributed throughout the temperate zones of Asia and Europe. Distribution ranges from the Himalayan region, India, Nepal, Bhutan, Pakistan, Afghanistan to China, Mongolia, Russia, Kazakhstan, Hungary, Romania, Switzerland, Germany, France and Britain to Scandinavian countries, including Finland, Sweden and Norway. In India, it is found in North West Himalayas.

The main chemical constituents include carotene and soluble sugars. The berries are rich in vitamin C content, and calcium, chromium, cobalt, iron, magnesium, manganese, molybdenum, potassium, sodium, strontium and zinc have been reported to be present. Malic and quinic acid are the major (>90%) organic acids present in fruit juice of species of different origin. The volatiles responsible for aroma include 3-methyl butanol, butyl pentanoate, 2-methyl propyl 3-methyl butanoate, ethyl 2-methyl butanoate and ethyl hexanoate. Quercetin, isorhamnetin, rhamnetin, steroids, terpenoids, alkaloids, fatty oil, etc. are also reported to be present. *Hippophae rhamnoides* has been widely used for the treatment of

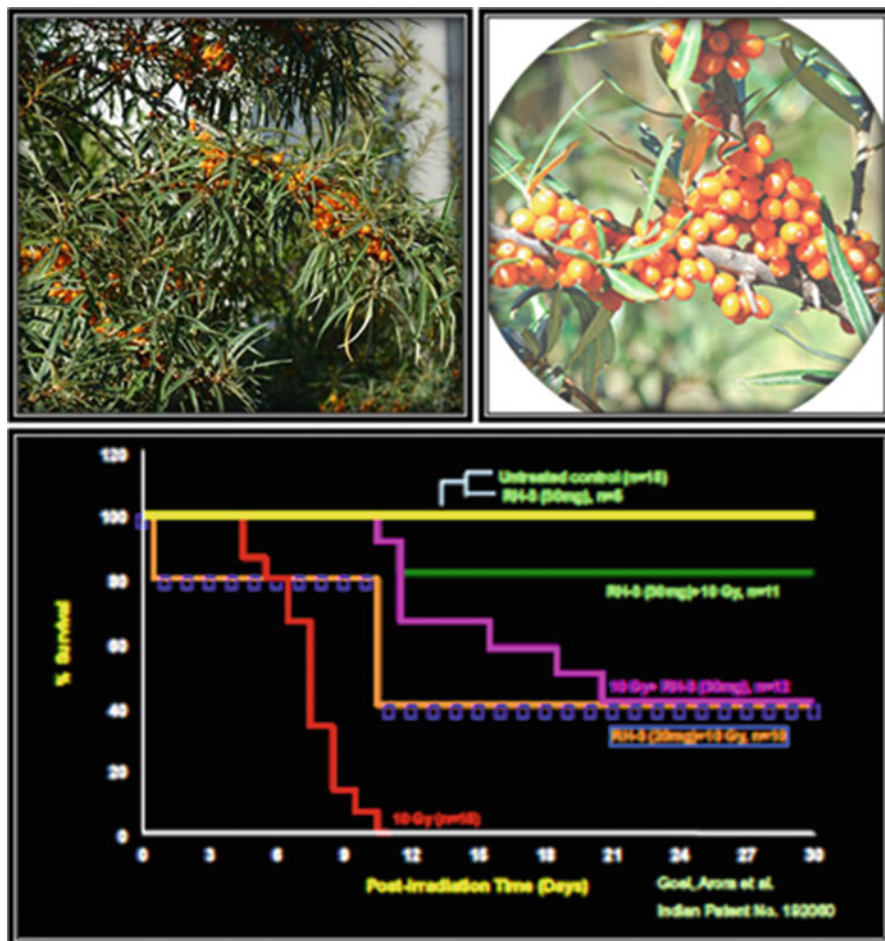


Fig. 26 *Hippophae rhamnoides* (sea buckthorn) – a promising radioprotector

circulatory disorders, vaginal mucositis, oral mucositis, wound healing, cutaneous eruptions, lung complaints, stomach malfunctioning, duodenal ulcers, cervical erosion, scalds, skin ulcers, hepatic injury, neoplasia and gastric cancers. It is also useful for treating skin ulcers, gastric disorders/cancers, mucositis, wounds and other high-altitude disorders. *Hippophae* has been shown to effectively protect mammals against lethal ionizing radiation and acts via multifarious ways, including free radical scavenging, immune modulation, boosting antioxidant defence, etc. *Hippophae* protects the haemopoietic system, gastrointestinal system and central nervous system against the deleterious effects of radiation and also mitigates gamma-radiation-induced genotoxicity (Swaroop et al. 2005, 2007; Chawla et al. 2007; Fig. 26). At molecular level, it has been shown that a large number of genes and proteins are modulated, thereby rendering radioprotection.

***Rhodiola imbricata* Edgew.**

Rhodiola imbricata Edgew. (roseroot or arctic root or golden root or shrolo) belongs to the family Crassulaceae and is an important medicinal plant and food crop of the Indian trans-Himalayan cold desert. It is an erect, perennial herb with rose-scented massive rootstock and fleshy, succulent stem. It has pale yellow flower which grows in clusters and is found at >4000 m in the high-altitude Himalayan ranges from Leh, Ladakh, India. It is also found in Pakistan and Nepal.

The biologically active phyto-constituents present in different *Rhodiola* species vary greatly according to the species. *Rhodiola* contains several bioactive compounds, e.g. phenolic glycosides, phenylpropanoids (rosavin, rosin, rosarin), flavonoids (rhodiolin, rhodionin, triclin, acetylrodalgin, catechins), proanthocyanidins (rhodioloside), tannins, phenylethanol derivatives (tyrosol), phenolic acids (chlorogenic, hydroxycinnamic, caffeic and gallic acid), monoterpenes (rosaridin, rosaridol), triterpenes (beta-sitosterol, daucosterol), etc. The plant has been in use in traditional systems of medicine since antiquity, where it has been used for treating a variety of ailments and also as a prophylactic and general tonic. The plant increases bodily endurance, work efficiency and longevity and is used to treat fatigue, asthma, fever, haemorrhage, depression, anaemia, impotence, gastrointestinal ailments, infections and central nervous system disorders. It is used for restoring memory and as a general health tonic and is also useful in cold, cough and lung ailments. In recent years, the plant has been used in Russia, Mongolia, China, India, America, Kazakhstan and European countries. The therapeutic uses include application in asthenic conditions like sleep disturbances, decline in work performance, loss of appetite, irritability and hypertension. It has been a widely accepted medicinal plant possessing antidepressant, tonifying, stimulative, DNA repair enhancing, anticancer, antimutagenic, reactive oxygen scavenging, adaptogenic, antiageing, antioxidant, anti-inflammatory, cardioprotective and central nervous system protective properties.

In a 30-day survival study, *Rhodiola imbricata* (Fig. 27) was found to be maximally effective at 400 mg/kg b.wt. administered 30 min prior to 10 Gy exposure in strain 'A' Swiss albino mice model system, 1000 mg/Kg b.wt. indicating the non-toxic behaviour of the extract (Arora et al. 2005a, 2008a, c, d; Chawla et al. 2010).

The reported therapeutic activities of *Rhodiola rosea*, a close species to *Rhodiola imbricata*, and the present study matched indicating that it is an excellent candidate for investigation of biological activity particularly related to radiation protection. Comparative analyses of the biological activities associated with the plant have also been performed. Simultaneously, screening of the novel compounds as well as the different reported categories of compounds from this plant species, presumably responsible for radioprotection, is also continuing. Studies have revealed the ability of extract to effectively tackle radiation-induced oxidative stress.

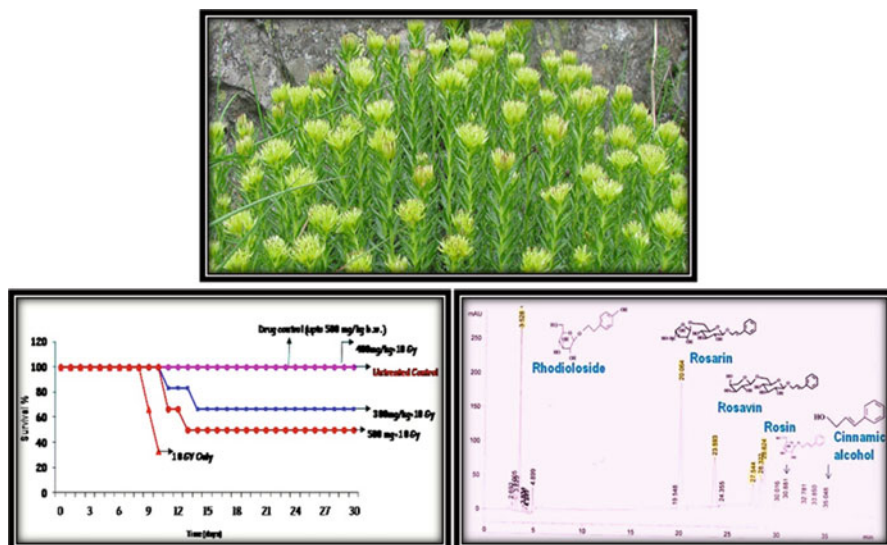


Fig. 27 Radioprotection by *Rhodiola imbricata* and identification of its key bioconstituents

***Ocimum sanctum* Linn. (Fig. 28)**

The radioprotective properties of tulsi (*Ocimum sanctum*) have been demonstrated at INMAS and taken to phase II clinical trials at the Advanced Centre for Treatment Research and Education at the Tata Memorial Centre in Mumbai. Undoubtedly, the preliminary results have been promising; however, the limitation of using total body irradiation as a clinical model for testing of radiation countermeasures has to be kept in mind, and its extrapolation to normal individuals who might be exposed to radiation needs to be considered in an unbiased manner. The radioprotectors developed at INMAS can ameliorate the adverse effects of radiotherapy in cancer patients and have immense potential.

Behavioural Radioprotectors

From a military perspective, behavioural radioprotectors are of immense importance since they can help improve the performance of soldiers and emergency first responders who may have to operate during crucial rescue and recovery missions during radiological/nuclear incidents. They can also be used by Air Force fighter pilots and in a naval setting. At INMAS, we have investigated *Centella asiatica*, *Zingiber officinale* and *Mentha piperita* and found them to render efficient behavioural radioprotection in rodent model system if administered prior to radiation



Fig. 28 Radioprotector from *Ocimum sanctum*

exposure (Goel et al. 2006; Haksar et al. 2006, 2009). A fairly narrow window of protection currently makes them appear suitable only for planned radiation exposures. However, their efficacy in postirradiation scenario and validation in higher animal models remains to be done.

Biotechnological Production of Radioprotective Molecules

As alluded to earlier, *P. hexandrum* (Himalayan mayapple) is an invaluable source of podophyllotoxin, 4'-demethylpodophyllotoxin, podophyllotoxin glycoside and other polyphenolic compounds that find application as anticancer, antiviral, antibacterial, immunostimulating and antirheumatic drugs. The aryltetralin lignans synthesized by the taxon are in great demand worldwide due to their use in the synthesis of topoisomerase inhibitors and form an integral part of the modern chemotherapeutic regimen for the treatment of a variety of cancers. The radioprotective and anti-HIV properties are further likely to increase the demand for lignans and related molecules produced by this important plant species. In order to maintain continued production of these aryltetralin lignans, the plant has to be harvested on a large scale from its natural environment, and this has resulted in the plant's endangered status, which now finds mention in the Red Data Book. The chemical synthesis of podophyllotoxin is complicated, and in view of the difficulties in its total chemical synthesis (due to the presence of four chiral centres along with a γ -lactone and a high degree of oxygenation), problems in cultivation on large scale and failure of metabolic engineering approaches, there is a need for alternative sources of production of aryltetralin lignans. To circumvent the problem of production of radioprotective secondary metabolites, a novel endophytic fungus (*Trametes hirsuta*) was isolated from high-altitude *P. hexandrum* with the capability to synthesize podophyllotoxin and other lignans and possessing amenability for scale-up in bioreactors (Puri et al. 2006; Fig. 29). Methodology for consistent production of the aryltetralin lignans was established, and methods for characterization by HPLC, LC-MS, LC/MS-MS and ¹H-NMR were developed and standardized. The lignans

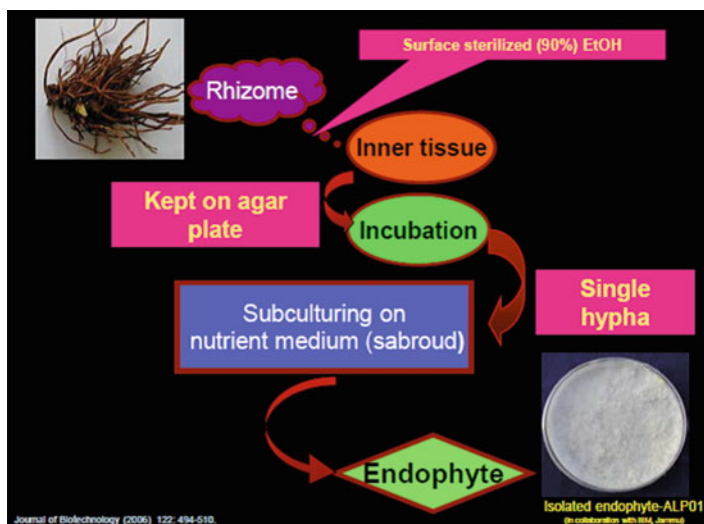


Fig. 29 Isolation of the endophytic fungus *Trametes hirsuta* from *Podophyllum hexandrum*

produced by the endophyte are biologically active and exhibited significant antioxidant, anticancer and radioprotective properties. This strategy promises to improve the production of these therapeutically important high-value bioactive radioprotective secondary metabolites at lower costs.

Biothreat Countermeasures

The rapid development of antimicrobial resistance amongst microbes poses serious public health concerns. As per the WHO, antibiotic resistance is a major threat to global health, food security and development in today's scenario. Though antibiotic resistance develops in microbes naturally, the extensive and indiscriminate use of antibiotics in humans and animals accelerates the process leading to the development of antibiotic resistance leading to plethora of microbes becoming drug-resistant posing grave concerns to humanity. Increasingly, diseases like pneumonia, tuberculosis and gonorrhoea are becoming harder to treat as the antibiotics used to treat them are becoming ineffective. Antibiotic resistance is fast becoming a major problem necessitating to longer stays in hospital and resulting in higher medical costs and increased mortality. Developing countries cannot afford the additional financial burden posed by this major problem. In addition, multidrug-resistant microbes can also pose biothreat concerns if used inappropriately by certain nefarious people to disrupt military as well as civil populations.

With antibiotic resistance becoming more prevalent and the consequent evolution of more virulent strains, there would be very few effective antimicrobial drugs available in our armamentarium to tackle antibiotic-resistant bacteria, and patients

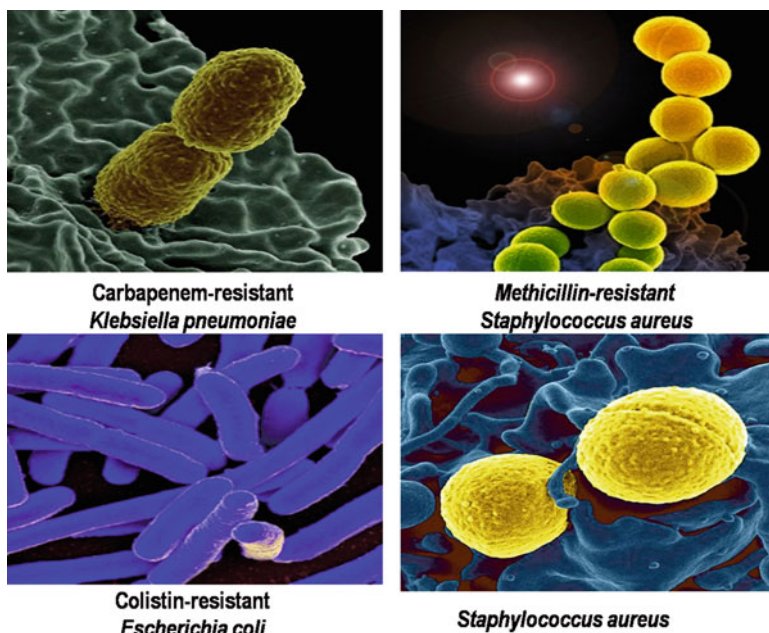


Fig. 30 The emergence of antibiotic resistance is a major challenge that needs to be tackled on priority basis (Photo Credit: National Institute of Allergy and Infectious Diseases, NIH)

might succumb to even simple infections as they would become untreatable. It is under such conditions that herbal medicine could be used as an alternative therapy for treatment.

Multiple drug resistance (MDR) refers to the resistance shown by a species of microorganism to multiple antimicrobial drugs. Several terms recognizing the varying degrees of MDR encountered have been introduced, e.g. drug resistant (XDR) and pandrug-resistant (PDR). A plethora of antibiotic-resistant bacteria have been reported, including community- and hospital-acquired methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-intermediate *S. aureus* (VISA), vancomycin-resistant enterococci, macrolide- and penicillin-resistant *Streptococcus pneumoniae*, extend-spectrum β -lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*, carbapenem-resistant Enterobacteriaceae (CREs) and multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter* spp. (Fig. 30).

The multidrug resistance offered by carbapenem-resistant *Escherichia coli* (CRE) (family: Enterobacteriaceae; class: Gammaproteobacteria) against third-line antibiotics can be attributed to its ability to develop biofilm(s). Such process involves adhesion and quorum-sensing induced colonization, leading to biomass development. Studies conducted at INMAS by our group have explored the anti-adhesion, anti-quorum sensing and anti-biofilm potential of 05 pre-standardized potent herbals

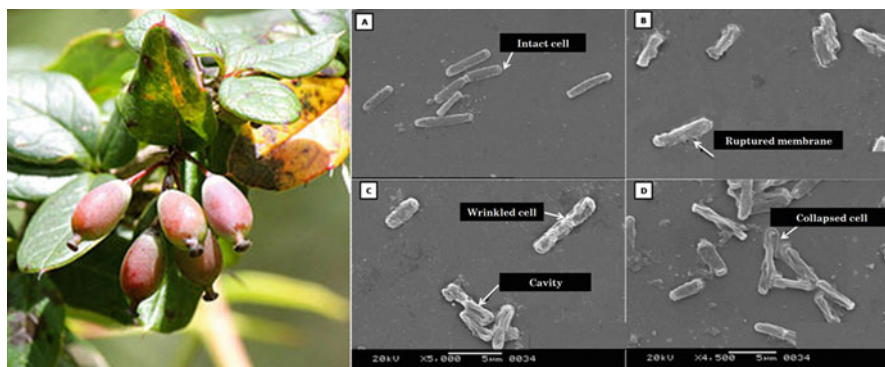


Fig. 31 Cell ultrastructure disruption as revealed by scanning electron microscopy upon treatment with *B. aristata*

(Thakur et al. 2016a,b). *Berberis aristata* (PTRC-2111-A) exhibited maximum potential vis-à-vis these activities, while *Holarrhena antidysenterica* (PTRC-8111-A) showed only anti-quorum sensing potential as compared to standards/antibiotics. These findings are in line with the molecular docking analysis of phytoligands against Lux S and Pilin receptors. Additionally, pairwise correlation analysis of the tested activities with qualitative, quantitative and bioactivity functional descriptors revealed that an increased content of alkaloid, moderate content of flavonoids and decreased content of tannins supported anti-adhesion, anti-quorum sensing and anti-biofilm potential activities. Besides, nitric oxide and superoxide scavenging activity correlated with anti-quorum sensing activity. The findings indicated clearly that *B. aristata* (family: Berberidaceae) and *C. sinensis* (family: Theaceae) are potent herbals with significant therapeutic potential for the management of CREs (Fig. 31).

Further we carried out studies using an aquo-ethanolic extract of *Camellia sinensis* (PTRC-31911-A), standardized using Fourier-transform infrared analysis, which revealed the presence of seven common functional groups (Thakur et al. 2016a,b). Combinations of PTRC-31911-A with third-line antibiotics (n = 5) were tested against carbapenem-resistant *Escherichia coli*. Combination modality revealed synergistic behaviour (fractional inhibitory concentration indices < 1) with tigecycline, ertapenem, meropenem, colistin and augmentin. The lead combination of PTRC-31911-A + ertapenem or meropenem showed maximum augmentative potential at a dose of 50 and 100 µg/mL, respectively, with nearly fivefold decrease in minimum inhibitory concentrations as compared with the respective antibiotics alone. The synergistic effects implied that the antibacterial combinations of PTRC-31911-A and ertapenem, meropenem, colistin, tigecycline or augmentin are more effective than monotherapy with either of these antibiotics.

Herbal Prophylactics and Therapeutic Agents: Preparing for Worst-Case Scenarios

Life-threatening opportunistic infections or biothreat agents can wreak havoc in individuals with inflammatory conditions if they are treated with available conventional therapies, and this has raised concerns in the management of national security (Tanwar et al. 2016). Highest priority opportunistic pathogens like *Salmonella species*, *Brucella abortus*, etc. pose a risk to national security as they can be easily disseminated or transmitted from person to person, which can further result in high mortality rates amongst the vulnerable populations. These pathogens in turn also play an important role in the initiation and perpetuation of such inflammatory conditions (e.g. rheumatoid arthritis and neurological disorders) in susceptible community. However, the use of biologic therapies (corticosteroids, NSAIDS, DMARDS) is also associated with increased risk of infections with intracellular microorganisms like *Salmonella spp.*, *E. coli*, etc. (Thakur et al. 2016a,b and Tanwar et al. 2017a,b). Further, the combination therapy of corticosteroids and conventional drugs like anti-inflammatory drugs (naproxen, aspirin, diclofenac) etc. was shown to have antagonistic effects. Nowadays, the management of inflammatory conditions requires aggressive treatment with existing conventional drugs. Due to an increase in the unwanted effects of such therapeutic modalities, alternative therapies, particularly herbal, need to be explored as a curative remedy for the management of such vulnerable condition in terms of ‘worst-case scenario’ (Thakur et al. 2016a). With this aim in mind, endeavours were made to identify and develop natural remedies that could be employed in worst-case scenarios (mainly in susceptible population) to modulate the deleterious effects of natural disease outbreaks or deliberate use of biothreat agents. A herbal informatics evidence-based matrix modelling approach was envisaged, and this unique approach utilized the in silico bioprospection for identification of potent herbal leads. The model was developed using PubMed-based dynamic search engines as interactive platform. The priority index algorithms were used as a basis for evaluation of relevance factor of various physiological targets or bioactivity parameters specific to a particular microorganism(s) or inflammatory condition(s) in conferring antibiotic resistance over a period of time (Chakotiya et al. 2016; Tanwar et al. 2017a,b). Similarly, the potential herbals identified the basis of classical bioprospection were subjected to binary, weightage and fuzzy set-based analysis using assigned relevance to each activity parameter as dependent variable. The final optimized matrix provided several potential herbal leads. These identified leads were further carried forward for evaluation of their antimicrobial activity as well as anti-inflammatory potential against a novel standardized ‘vulnerable animal model’ (collagen type II-induced rheumatoid arthritis in combination with opportunistic infections involving multidrug resistant pathogens as worst-case scenario) (Tanwar et al. 2017a,b). The identified herbal leads (e.g. *Camellia sinensis*, *Berberis aristata*, etc.) could be utilized as novel holistic drugs in the future for the management of biothreats posed, particularly in vulnerable populations.

Broad-Spectrum Antiviral Drugs

There is a dearth of antiviral drugs in modern systems of medicine due to the rapid rate of mutation found in viruses. Viral pathogens pose a serious threat, especially the clinical viruses (HIV, hepatitis viruses, etc.), natural emerging viruses (avian and swine influenza strains, SARS, novel H1N1, H1N5, etc.) and viruses relevant to potential bioterrorism (Ebola, smallpox, etc.) (Rider et al. 2011). Unfortunately, there are relatively few prophylactics or therapeutics available for management of viral diseases and pandemics (Arora et al. 2010f, 2011). A plethora of medicinal plants exhibit promise for the treatment of viral infections, as several of them possess potent broad-spectrum antiviral activity (Arora et al. 2011, 2013). In the past, evaluation of antiviral activity of medicinal plants was constrained in view of the highly infectious nature of viruses and lack of suitable separation techniques for the identification of antiviral components. Development of vector-based strategies, in which non-infectious molecular clone of a virus is used for antiviral screening purposes and advancement in separation technologies, has offered promise for medicinal plants usage in modern antiviral drug discovery (Mukhtar et al. 2008). With increase in the virulence of viruses, emergence of new viral strains and non-availability of broad-spectrum synthetic drugs, there is a need to explore plants for the development of new and potent antiviral drugs.

DRDO has been engaged in the development of new candidate drugs for treating viral infections. *Hippophae rhamnoides* has been tested for its anti-dengue potential (Jain et al. 2008). Dengue virus occurs as four distinct serotypes, viz. dengue 1, 2, 3 and 4. Symptomatic dengue virus infection ranges from a self-limited febrile illness and dengue fever to a more severe disease, dengue haemorrhagic fever/dengue shock syndrome. Medical treatment of dengue poses serious issues as virtually no targeted therapeutic agents are available to treat the disease and consequently whatever treatment is given is mostly supportive in nature. Jain et al. (2008) evaluated the anti-dengue activity of *Hippophae rhamnoides* leaf extract in dengue virus type II infected blood-derived human macrophages. The dengue virus-infected cells were treated with *Hippophae rhamnoides* leaf extract and compared with the commercially available antiviral drug – ribavirin. The extract was able to maintain the cell viability of dengue-infected cells at par with ribavirin, along with the decrease and increase in TNF- α and IFN- γ , respectively. Anti-dengue activity of *Hippophae rhamnoides* extract was further determined by the traditional plaque assay. The results suggested that the *Hippophae rhamnoides* leaf extract has significant anti-dengue activity and has potential for the treatment of dengue.

Understanding and modulating the signal transduction pathways are imperative to the development of new therapeutic agents. It is well known that the recognition of virus infection by retinoic acid-inducible gene (RIG) I and melanoma differentiation-associated protein (MDA) 5, which are RNA helicases, and interferon-stimulated gene (ISG) 15 can activate a cascade of signal transduction pathways leading to production of type I interferons and proinflammatory cytokines that synchronize the removal of the virus from the host. However, it has been demonstrated that RNA-helicase-mediated innate immunity plays an important role in defending the host

from infection. During endeavours to identify plant-derived antivirals that could selectively enhance ISG- and RNA-helicase-mediated antiviral immune responses, *Rhodiola* was found to be effective. *Rhodiola* treatment significantly promoted ISG, RIG-I and MDA 5 gene expression and an antiviral immune response against dengue virus infection. *Rhodiola* treatment also induced interferon (IFN) β and other cytokines, including IL-1 β , TNF- α , IL-6 and IL-8 in infected cells. *Rhodiola* also upregulated phosphorylated eIF-2 α , PKR and NF- κ B in infected cells. In addition, the number of NK cells was also increased upon treatment with *Rhodiola* in dengue virus-infected human PBMCs. Based on the studies, Diwaker et al. (2014) demonstrated that *Rhodiola* induces pharmacological modulation of RIG-I, MDA 5 and ISG signal transduction pathways supporting the induction of a favourable antiviral immune response against dengue virus and, can, therefore, be a novel therapeutic strategy for the management of dengue infection.

Chemical Warfare Countermeasures

Chemical warfare agents (CWAs) and toxic industrial chemicals (TICs) can pose problems during military conflicts and terrorism since most CWA and TIC exposures are difficult to manage as these agents have a rapid onset of action and can kill, injure or incapacitate human beings within no time. The mostly unprepared individuals get affected almost immediately; the first responders can get accidentally exposed, and the population in the vicinity can get affected rapidly. The specific mode of toxicity of these agents is varied; they are often mediated either directly or indirectly with increased oxidative stress in biological systems. Consequently, a plethora of antioxidants have been explored as potential medical countermeasures for CWA/TIC exposures. In DRDO, studies have been performed with a diverse array of CWAs, model organisms, exposure systems, target organs and antioxidants, looking at an almost equally assorted set of endpoints. Endeavours at treating CWAs/TICs with antioxidants have often met with mixed results, though exploration of antioxidants as medical countermeasures for CWA/TIC management has shown some potential. A plethora of herbal drugs have been utilized for their protective efficacy against chemical warfare agents, including extremely toxic sulphur mustard (SM). Ethanolic extract of *Hippophae rhamnoides* leaf (HL-EOH), water and ethanolic extract of *H. rhamnoides* fruit (HF-W and HF-EOH) and *H. rhamnoides* flavone from fruit (HR-flavone) were evaluated against percutaneously administered sulphur mustard (Vijayaraghavan et al. 2006). The *H. rhamnoides* extracts (1 g/kg; 3 doses; po) significantly protected SM-induced lethality. Following percutaneous administration of sulphur mustard, reduced glutathione and oxidized glutathione levels decreased, and malondialdehyde was elevated. Oral administration of HL-EOH and HR-flavone significantly protected

against loss of body weight. Following oral administration of ethanolic leaf extract and HR-flavone, recovery GSH, GSSG and MDA levels were recorded. The authors concluded that percutaneous administration of sulphur mustard induces oxidative stress, and ethanolic extract of leaf of *H. rhamnoides* and *H. rhamnoides* flavone from fruit can significantly protect against sulphur mustard-induced toxicity.

Prophylactic effect of gossypin (3,3',4',5,7,8-hexahydroxyflavone 8-glucoside) – an anti-inflammatory compound widely used as a herbal remedy for treating diabetes, jaundice, inflammation melanoma and glioma – has been demonstrated against percutaneously administered sulphur mustard in mice (Gautam and Vijayaraghavan 2007).

Various antioxidants like trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) and quercetin have been shown to protect the liver and lung tissues from oxidative damage caused by sulphur mustard exposure through inhalation and percutaneous routes (Kumar et al. 2001). This study showed that antioxidants could enhance survival time, protect the liver and lung from oxidative damage and reduce accumulation of purine metabolites in the blood following SM intoxication.

Conserving and Harnessing Natural Resources in Extreme Terrain

Defence Institute of High Altitude Research (DIHAR) has established a permafrost-based plant germplasm storage facility and modern laboratory at Chang La top (5360 m AMSL) in Ladakh exploiting the naturally existing sub-zero temperature in the region for most parts of the year (Fig. 32). The facility provides an insurance against both incremental and catastrophic loss of the plant diversity. The preserved diversity of the genes will serve as a safety net for current and future food security in an era of global warming and climate change. The facility is being utilized by DRDO and ICAR for storage of germplasm of economically important plant species for posterity. The facility will serve as a backup of important germplasm for posterity.



Fig. 32 Permafrost facility at Chang La with modern laboratories at a height of 17,600 ft AMSL

Improving Health and Well-Being of Armed Forces Personnel and Spin-Offs for Civil Applications

Vector Control

The Indian Armed Forces personnel are deployed at various locations and different geoclimatic locales. They are constantly exposed to a variety of bloodsucking insects such as mosquitoes, blackflies, ticks, mites, rat flea, sandflies and leeches during their operational postings. Insects are carriers (vectors) of dreaded diseases such as malaria, dengue, chikungunya, etc. Various methods have been used for the ecological condition with certain limitations. Application of insecticide residual spraying causes inconvenience to children and older persons and can cause toxicity. A better method would be to use personal protection measures to protect human from the painful bites of bloodsucking organisms such as mosquito, sandfly, blackfly, rat flea and bedbugs.

Amongst vectors, mosquitoes are responsible for causing major vector-borne diseases in India and other tropical countries. Use of repellents and insecticides is the best possible methods to keep mosquitoes at bay. Synthetic repellents used in commercially available mosquito kits are toxic to human health and detrimental to environment. A herbal mosquito repellent has been formulated using six essential oils of indigenous plant species which can be used with the help of vapourizing kit (Fig. 33). It is a formulation of essential oils of traditional herbs, is non-toxic as compared to the commercially available products, has natural fragrance and is eco-friendly. The herbal formulation wards off insects and, therefore, has immense potential for use in hot and humid areas, where vector-borne diseases are most prevalent.

The mosquito repellent formulation derived from local herbs has been value added with natural fragrance for using as mosquito-cum-room freshener (Aeromos). It has an extra advantage over conventional mosquito repellents available in the market due to additional natural fragrance. It can be used as mosquito repellent as well as a deodorant by spraying in the living rooms. It is primarily a formulation of



Fig. 33 Mosquit: an eco-friendly, herbal mosquito repellent (left) and Aeromos (right)

Fig. 34 Bio-larvicide for controlling mosquito larvae at the breeding sites



essential oils of local herbs and is effective for 3–4 h, non-toxic and eco-friendly, and the natural fragrance is acceptable to all age groups.

Control of mosquito-borne diseases at larval stage is said to be one of the best approaches to limit the control of diseases. With this aim, Defence Research Laboratory (DRL), Tezpur, has isolated a bioactive entomopathogenic bacterium, *Bacillus sphaericus* GC Sub Gr. IV, which is effective against mosquito larvae. The isolated bacterium has been formulated as a bio-larvicide for controlling mosquito larvae at the breeding sites (Fig. 34). The bio-larvicide is derived from nature and is eco-friendly, and the effective dose rate of the formulation is 0.1–0.2 kg/ha.

Herbal Adjuvant to Increase Vaccine Response

Adjuvants are substances that act to accelerate, prolong or enhance antigen-specific immune responses when used with specific vaccine antigens. A herbal adjuvant is an agent of natural origin that may stimulate the immune system and increase the response to a vaccine, without having any specific antigenic effect in itself. Adjuvants have been used for decades as important agents for generation of strong immune response to vaccine antigens. Besides generating strong immune response, they also act as immunomodulators by influencing the type and character of antibody generated. Defence Institute of Physiology and Allied Sciences (DIPAS) has developed a new herbal adjuvant, called DIP-HIP (Fig. 35), and compared its efficacy to standard adjuvants, viz. complete Freund's adjuvant and alum.

Antigen-specific immunoglobulin levels have shown to be significantly enhanced by DIP-HIP. Upon administration of DIP-HIP, cytokine profile correlates well with the Th1 and Th2 type of immune response. Immunization through different routes like intraperitoneal and intramuscular did not show any significant difference nor caused any muscular damage, granulomatous reaction or dystrophy. The shelf life of DIP-HIP is more than 3 years, whereas in the formulation with antigen, it is about 4 months at 40 ° C. No haemolytic activity is observed on the treatment of both human and animal erythrocytes with DIP-HIP. Incorporation of DIP-HIP results in

Fig. 35 A novel herbal adjuvant for increasing vaccine response



enhancing, accelerating and prolonging the antigen specific-antibody responses in animals. Further advantages of DIP-HIP include enhancement of immunogenicity, reduction of antigen amount needed for a successful immunization and reduction of frequency of booster immunization, without any muscular damage or side effects.

Herbal Hypolipidemic

A herbal hypolipidemic DIP-LIP has been obtained from a high-altitude growing plant. It is rich in essential fatty acids like linoleic acid (26%), linolenic acid (20%) and other important fatty acids such as oleic (30%) and palmitic acid (17%). The presence of these fatty acids and total carotenoids (430 ppm) and tocopherol (1175 ppm) imparts potent bioactivities. DIP-LIP has significant hypocholesterolemic activity and inhibits cholesterol deposition in cholesterol-fed animals, besides increasing HDL cholesterol levels. DIP-LIP also exhibits significant vasorelaxant activity in aortic ring model. DIP-LIP also increases resistance to hypoxia and cold stress. DIP-LIP can be widely used for atherosclerotic cases and for its hypolipidemic and vasorelaxant properties.

Anti-vitiligo Herbal Ointment and Oral Liquid

Vitiligo or leucoderma is a chronic auto-immune dermal disease with virtually no reasonably effective treatment available in modern system of medicine. Frequently even systemically administered steroids are not effective. It is a social stigma and is caused mainly due to decreased synthesis of melanin pigment by the skin resulting in white patches and discolouration of the affected areas. The current treatment

modalities have not been able to provide any satisfactory solution. Defence Institute of Bioenergy Research (DIBER) has developed a polyherbal topical cream and oral mixture of seven herbs (lukoskin) for curing vitiligo without side effects upon long-term application (Fig. 36). The combination therapy was found to inhibit reoccurrence of white patches besides preventing blister formation and has no side effects. Lukoskin enhances melanin synthesis, is a non-toxic herbal product and prevents hyper pigmentation and restores normal skin texture.

Herbal Anti-Eczema Ointment

Eczema or atopic dermatitis is an eruption of the skin characterized by pinhead-sized maculae, papules and vesicles accompanied by intolerable itching. The vesicles and papules exude yellowish material forming crusts which on scratching can bleed and secondary infection may set in. There is a seasonal relapse, and also all the clinical features need separate drugs. A polyherbal ointment (Eczit; Fig. 37) has been developed and found to address all clinical features of eczema, including psoriasis. Topical application of this preparation is effective in all kinds of eczema and devoid of any side effects. The formulation is low cost and broad spectrum and is a non-toxic



Fig. 36 Anti-vitiligo herbal formulation – lukoskin



Fig. 37 Eczit (herbal anti-eczema ointment)

polyherbal ointment. The product offers better efficacy than the product in the market, is effective in all kinds of eczema, stops reoccurrence and has no side effects.

Antioxidant Beverages and Supplements

Antioxidant beverages and supplements have been developed utilizing the medicinal plants grown in the Himalayan region. Seapricot is cloud-stable blended herbal beverage based on the pulp of sea buckthorn (*Hippophae rhamnoides*) and apricot (*Prunus armeniaca*). The blended herbal beverage is rich in vitamins, unsaturated fatty acids, carbohydrate, proteins, minerals, etc., which is the synergistic effect of both the fruits, having antioxidant, nutraceutical and health refreshing properties. The blended herbal beverage – seapricot – does not contain any hydrocolloids and artificial colour or flavour. The beverage has antioxidant properties and is rich in vit A, vit B₁, vit B₂, vit B₃, vit B₆, vit B₉ vit B₁₂, vit 'C', vit 'E' and unsaturated fatty acids (Fig. 38).

An 'antioxidant herbal nutraceutical supplement' based on sea buckthorn and other fruit pulp and extracts of high-altitude medicinal plants has been developed. The detailed nutritional profiling of the herbal antioxidant supplement has been conducted and found to be rich in various vitamins, unsaturated fatty acids, etc. Acute and subacute oral toxicity studies on the product were carried out, and no toxicity was found. The heavy metals, viz. arsenic, cadmium, mercury and lead, were found below detection level. The main ingredients are *Hippophae* sp., *Emblica* sp., *Rhodiola* sp., *Origanum* sp., *Capparis* sp., *Achillea* sp., *Rubia* sp., *Prunus* sp., etc. The supplement developed is rich in vit 'C' (124 mg/100gm), vit 'A' (121 IU/100 ml), vit 'B' complex, vit 'E', minerals, unsaturated fatty acids, minerals, etc.



Fig. 38 Seapricot beverage, herbal antioxidant supplement and antihypertensive beverage – Hridayamrith

An antihypertensive beverage – Hridayamrith – has been developed from Himalayan shrub, viz. *Crataegus crenulata*. Hridayamrith is a herbal cardiac tonic and is useful in case of hypertension, angina, arrhythmia and congestive heart failure. It is an energizer, nerve soothing and refresher health tonic. The presence of flavonoids in this beverage helps in cardiotropic and vasodilator action. The regular intake of drink lowers the serum cholesterol and triglycerides.

Challenges and Issues Ahead

For several terrain, operation and platform-specific problems faced by our Armed Forces, there are no effective solutions available. DRDO has been making concerted efforts to consolidate and streamline research and development endeavours on herbal products to provide unique solutions to the Armed Forces. In the process, at times some spin-offs emanate, which find practical application in both military and civil setting. With a view to meeting emerging challenges, the traditional knowledge on herbs of high altitudes, desert areas, Central Himalayan and North East region, etc. is being documented, and research carried out to generate scientific data that can be useful for the Armed Forces. There is a paradigm shift towards acceptance of scientifically validated herbals as effective prophylactic and therapeutic agents. The grant of the 2015 Nobel Prize in Physiology or Medicine to discoveries concerning novel therapies for some of the most devastating parasitic diseases, viz. river blindness, lymphatic filariasis (elephantiasis) and malaria, has once again highlighted the importance that herbal drugs are receiving in today's world. Drugs derived from *Streptomyces avermitilis* and *Artemisia annua* were found to be effective against parasitic diseases. However, it is a paradox that in our country, where Ayurveda has been a very successful and effective system of medicine for over 5000 years, there is still some amount of scepticism among civil health experts when it comes to acceptance of herbal drugs, and services are no exception.. This

view has to change in coming times if the full benefit of scientifically validated herbal drugs has to reach the users. The realization that herbal drugs are effective and safe and can solve the emerging problems of our Armed Forces will lead to induction of more and more products to the advantage of our soldiers who operate in harsh and extreme terrain and inhospitable operational conditions. As alluded to earlier, serious endeavours are underway in DRDO towards protecting the warfighter and promoting performance through the development of scientifically validated herbal products, processes and technologies. The need of the hour is achieving greater synergy with the services and industrial partners so that the herbal products, technologies and complementary and alternative medicine can be inducted in a rapid manner for the benefit of the soldiers.

Disclaimer

The views and opinions expressed in this article are entirely those of the author and do not necessarily reflect the official policy or position of DRDO/Government of India. The article contains only unclassified information, and the pictures have been used for representative purposes only. No endorsement of any private company or enterprise is made, as ToT in DRDO is done on a non-exclusive basis. Any herbal technology that has been left out is purely unintentional and is mainly due to space and other constraints.

Acknowledgements The author is grateful to his numerous co-workers and students in various Life Sciences cluster of laboratories of DRDO, colleagues in the Directorate General-Life Sciences, DRDO Headquarters and Directors of various Life Sciences cluster of laboratories. The author is thankful to the present and former Director General-Life Sciences and Secretary, Department of Defence R&D and Chairman, DRDO for encouragement, support and facilitation in multifarious ways.

References

- Arora R, Chawla R, Jaiswal S, Kumar R, Chawla R, Sagar R, Prasad J, Singh S, Kumar R, Sharma A, Singh S, Sharma RK (2005a) Evaluation of radioprotective activities of *Rhodiola imbricata*-A high altitude plant. *Mol Cell Biochem* 273:209–223
- Arora R, Gupta D, Chawla R, Prasad J, Singh S, Sharma AK, Kumar R, Sagar RK, Samanta N, Sharma RK (2005b) Radioprotection by plant products: present status and future prospects. *Phytother Res* 19:1–22
- Arora R, Kumar R, Sharma AK, Prasad J, Singh S, Sagar RK, Chaudhary P, Shukla S, Kaur G, Sharma RK, Puri SC, Handa G, Gupta VK, Qazi GN (2005c) Antioxidant activities of fractionated extracts of high altitude *Podophyllum hexandrum* in radiation protection. *Mol Cell Biochem* 273:193–208
- Arora R, Chawla R, Puri SC, Sagar RK, Singh S, Kumar R, Sharma AK, Prasad J, Singh S, Kaur G, Chaudhary P, Qazi GN, Sharma RK (2005d) Radioprotective and antioxidant activity of low altitude *Podophyllum hexandrum*. *J Environ Pathol Toxicol Oncol* 24(4):299–314
- Arora R, Chawla R, Singh S, Sagar RK, Kumar R, Sharma AK, Singh S, Prasad J, Sharma RK, Tripathi RP (2006) Radioprotection by Himalayan high-altitude region plants. In: Sharma RK,

- Arora R (eds) Herbal drugs: a twenty first century perspective. Jaypee Brothers Medical Publishers (P) Ltd., Delhi, pp 301–325
- Arora R, Chawla R, Singh S, Sagar RK, Kumar R, Sharma A, Prasad J, Singh S, Gurudatta GU, Sharma RK (2007a) Bioprospection for radioprotective molecules from indigenous flora. In: Govil JN, Singh VK, Bhardwaj R (eds) Recent progress in medicinal plants. Studium Press, New York, pp 179–219
- Arora R, Lata M, Prasad J, Singh S, Kumar R, Singh L, Choudhary P, Sagar RK, Singh S, Kumar R, Singh S, Prasad J, Puri SC, Qazi GN, Krishan B, Sharma RK, Tripathi RP (2007b) Cytoprotective effect of *Podophyllum hexandrum* against γ - radiation is mediated via hemopoietic stimulation and up-regulation of heme-oxygenase-1 and the prosurvival multidomain protein BCL-2. *Integr Cancer Ther* 6(1):54–65
- Arora R, Kumar R, Sharma A, Tripathi RP (2008a) Radiomodulatory compounds of herbal origin for new frontiers in medicine, homeland security, management of radiological incidents and space applications. In: Arora R (ed) Herbal radiomodulators: applications in medicine, homeland defence and space. CABI Publishing, Wallingford, pp 1–22
- Arora R, Singh S, Puri SC, Sharma RK (2008b) Himalayan Mayapple (*Podophyllum hexandrum* Royle): traditional uses, clinical indications and future prospects. In: Watson RR, Preedy VR (eds) Botanical medicine in clinical practice. CABI Publishing, Wallingford, pp 71–84
- Arora R, Sharma A, Kumar R, Tripathi RP (2008c) Herbal radiation countermeasure agents: promising role in the management of radiological/nuclear exigencies. *Radiat Prot Environ* 31(1-4):304–306
- Arora R, Singh S, Sagar RK, Chawla R, Kumar R, Puri SC, Singh S, Prasad J, Gupta ML, Krishna B, Siddiqui MS, Sharma AK, Tripathi RP, Qazi GN, Sharma RK (2008d) Radiomodulatory and free radical scavenging activity of the fractionated extract of the adaptogenic nutraceutical (*Rhodiola*) – a comparative in vitro assessment with ascorbate. *J Diet Suppl* 5(2):147–163
- Arora R, Kumar R, Sharma A, Prasad J, Singh S, Gupta D, Sharma RK, Tripathi RP (2009) Radiation countermeasure agents from novel high-altitude Himalayan herbs: promise and prospects. *Indian J Radiat Res* 6(1-2):33–36
- Arora R, Chawla R, Dhaker AS, Adhikari M, Sharma J, Singh S, Gupta D, Kumar R, Sharma A, Sharma RK, Tripathi RP (2010a) *Podophyllum hexandrum* as a potential botanical supplement for the medical management of nuclear and radiological emergencies (NREs) and free radical-mediated ailments: leads from in vitro/in vivo radioprotective efficacy evaluation. *J Diet Suppl* 7(1):31–50
- Arora R, Gupta D, Chawla R, Adhikari M, Sharma J, Dhaker AS, Goyal V, Kumar R, Sharma A, Sharma RK, Tripathi RP, Puri SC (2010b) Antioxidant, anticancer, cytoprotective and radioprotective properties of Indian *Podophyllum hexandrum*. In: Arora R (ed) Herbal medicine: a cancer chemopreventive and therapeutic perspective. Jaypee Brothers Medical Publishers (P) Ltd., Delhi, pp 616–630
- Arora R, Malhotra P, Chawla R, Gupta D, Juneja M, Kumar R, Sharma A, Baliga MS, Sharma RK, Tripathi RP (2010c) Herbal drugs for oncology: current status and future directions in cancer chemoprevention. In: Arora R (ed) Herbal medicine: a cancer chemopreventive and therapeutic perspective. Jaypee Brothers Medical Publishers (P) Ltd., Delhi, pp 3–41
- Arora R, Chawla R, Marwah R, Kumar V, Goel R, Arora P, Jaiswal S, Sharma RK (2010d) Medical radiation countermeasures for Nuclear and Radiological Emergencies (NREs): current status and future perspectives. *J Pharm Bioallied Sci* 2(3):202–212
- Arora R, Dhaker AS, Gupta D, Chawla R, Adhikari M, Singh S, Sagar R, Kumar R, Sharma A, Sharma RK, Puri SC, Sultana S, Mathur AK, Qazi GN, Ahuja PS, Tripathi RP (2010e) Natural bioresource of the North Himalayan Region as a source of promising radiation countermeasure agents: lessons from *Podophyllum hexandrum*. In: Gupta VK (ed) Comprehensive natural products: potential and challenges. Studium Press, Houston, pp 131–156
- Arora R, Goel R, Singh S, Kaushik V, Singh PK, Chhabra V, Bhardwaj JR (2010f) Mitigation approaches to combat Flu Pandemic. *J Global Infect Dis* 1(2):117–130

- Arora R, Chawla R, Sharma RK (2010g) Himalayan bioresource *Rhodiola imbricata* as a promising radiation countermeasure agent for nuclear and radiological emergencies. *J Pharm Bioallied Sci* 2(3):213–219
- Arora R, Shivashankara AR, Azmidah A, Haniadka R, Rai MP, Malhotra P, Sundriyal S, Yashavanth HS, Pai RJ and Baliga MS (2011) Medicinal plants as remedies for gastrointestinal ailments and diseases: a review. *Bioactive foods and chronic disease states*. Ronald Watson, Elsevier, Wageningen.
- Arora R, Malhotra P, Sundriyal S, Yashavanth HS, Pai RJ and Baliga MS (2013) Chapter 19: Medicinal Plants as Remedies for Gastrointestinal Ailments and Diseases: a Review A2 - Watson, Ronald Ross. In: Preedy VR (ed) *Bioactive Food as Dietary Interventions for Liver and Gastrointestinal Disease*, Academic Press, San Diego, pp 301–311
- Chadha V (2005) *Low intensity conflicts in India: an analysis*. Sage Publications Private Ltd, New Delhi, p 513
- Chakotiya AS, Chawla R, Thakur P, Tanwar A, Narula A, Grover SS, Goel R, Arora R, Sharma RK (2016) In vitro bactericidal activity of promising nutraceuticals for targeting multidrug resistant *Pseudomonas aeruginosa*. *Nutrition* 32(7-8):890–897
- Chatterjee A, Pakrashi SC (1996) *The treatise on Indian medicinal plants, vol 1*. Publications & Information Directorate, CSIR, New Delhi
- Chawla R, Arora R, Kumar R, Sharma A, Prasad J, Singh S, Sagar R, Chaudhary P, Shukla S, Kaur G, Sharma RK, Puri SC, Dhar KL, Handa G, Gupta VK, Qazi GN (2005a) Antioxidant activity of fractionated extracts of rhizomes of high-altitude *Podophyllum hexandrum*: role in radiation protection. *Mol Cell Biochem* 273(1-2):193–208
- Chawla R, Arora R, Sagar RK, Singh S, Puri SC, Kumar R, Singh S, Sharma AK, Prasada J, Khan HA, Sharma RK, Dhar KL, Spitteller M, Qazi GN (2005b) 3-O-beta-D-Galactopyranoside of quercetin as an active principle from high altitude *Podophyllum hexandrum* and evaluation of its radioprotective properties. *Z Naturforsch C* 60(9-10):728–738
- Chawla R, Arora R, Singh S, Sagar RK, Sharma RK, Kumar R, Sharma A, Tripathi RP, Puri SC, Khan HA, Shawl AS, Sultan P, Krishan T, Qazi GN (2006) *Podophyllum hexandrum* offers radioprotection by modulating free radical flux: role of aryl-tetralin lignans. *Evid Based Complement Alternat Med* 3(4):503–511
- Chawla R, Arora R, Singh S, Sagar RK, Sharma RK, Kumar R, Sharma A, Gupta ML, Singh S, Prasad J, Khan HA, Swaroop A, Sinha AK, Gupta AK, Tripathi RP, Ahuja PS (2007) Radioprotective and antioxidant activity of fractionated extracts of berries of *Hippophae rhamnoides*. *J Med Food* 10(1):101–109
- Chawla R, Jaiswal S, Kumar R, Arora R, Sharma RK (2010) Himalayan Bioresource *Rhodiola imbricata* as a promising radioprotector for nuclear and radiological emergencies. *J Pharm Bioallied Sci* 2(3):213–219
- Diwaker D, Mishra KP, Ganju L et al (2014) *Rhodiola* inhibits dengue virus multiplication by inducing innate immune response genes RIG-I, MDA5 and ISG in human monocytes. *Arch Virol* 159(8):1975–1986
- Gautam A, Vijayaraghavan R (2007) Prophylactic effect of gossypin against percutaneously administered sulfur mustard. *Biomed Environ Sci* 20(3):250–259
- Goel HC, Prasad J, Sharma A, Singh B (1998) Antitumour and radioprotective action of *Podophyllum hexandrum*. *Indian J Exp Biol* 36(6):583–587
- Goel HC, Arora R, Prasad J et al (2000a) A process for preparation of a radioprotective herbal extract-I. Indian Patent filed. Patent Office, New Delhi
- Goel HC, Prasad J, Sharma AK, Singh S, Mathew TL, Chaurasia OP, Singh B (2000b) A process for preparation of a radioprotective herbal extract-II. Indian Patent filed. Patent Office, New Delhi
- Goel, HC, Arora R, Shobi V, Mathew TL (2006) A Process for Preparation of a Behavioural Radioprotective Herbal Extract. Indian Patent (no. 194325)

- Grover SK, Divekar HM, Kumar R, Pahwa ML, Bhardwaj SK, Gupta AK, Srivastava KK (1995) Experimental evaluation of Composite Indian Herbal preparation II (CIHP II) as an adaptogen and its mechanism of action. *Int J Pharmacognosy* 33:148–154
- Gupta D, Arora R, Garg AP, Goel HC (2003) Radiation protection of HepG2 cells by *Podophyllum hexandrum* Royale. *Mol Cell Biochem* 250(1-2):27–40
- Gupta D, Arora R, Garg AP, Bala M, Goel HC (2004) Modification of radiation damage to mitochondrial system in vivo by *Podophyllum hexandrum*: mechanistic aspects. *Mol Cell Biochem* 266(1-2):65–77
- Gupta ML, Agrawala PK, Kumar P, Devi M, Soni NL, Tripathi RP (2008) Modulation of gamma radiation-inflicted damage in Swiss albino mice by an alcoholic fraction of *Podophyllum hexandrum* rhizome. *J Med Food* 11(3):486–492
- Haksar A, Sharma A, Chawla R, Kumar R, Arora R, Singh S, Prasad J, Gupta M, Tripathi RP, Arora MP, Islam F, Sharma RK (2006) *Zingiber officinale* exhibits behavioral radioprotection against radiation-induced CTA in a gender-specific manner. *Pharmacol Biochem Behav* 84(2):179–188
- Haksar A, Sharma A, Chawla R, Kumar R, Lahiri SS, Islam F, Arora MP, Sharma RK, Tripathi RP, Arora R (2009) Mint oil (*Mentha spicata* Linn.) offers behavioral radioprotection: a radiation-induced conditioned taste aversion study. *Phytother Res* 23(2):293–296
- Jain M, Ganju L, Katiyal A, Padwad Y, Mishra KP, Chanda S, Karan D, Yogendra KMS, Sawhney RC (2008) Effect of *Hippophae rhamnoides* leaf extract against Dengue virus infection in human blood-derived macrophages. *Phytomedicine* 15(10):793–799
- Krysa-Clark J, Lewis S, Waterworth TA (2004) Management of a snake bite in the field. *J R Army Med Corps* 150:97–98
- Kumar R, Grover SK, Shyam R, Divekar HM, Gupta AK, Srivastava KK (1999) Enhanced thermogenesis in rats by a Composite Indian Herbal Preparation-I and its mechanism of action. *J Altern Complement Med* 5:245–251
- Kumar R, Shyam R, Divekar HM, Pahwa ML, Srivastava KK (2000) Mechanism of increased tolerance to hypothermia after Composite Indian Herbal Preparation II administration. *J Altern Complement Med* 6:509–517
- Kumar O, Sugendran K, Vijayaraghavan R (2001) Protective effect of various antioxidants on the toxicity of sulphur mustard administered to mice by inhalation or percutaneous routes. *Chem Biol Interact* 134(1):1–12
- Mukhtar M, Arshad M, Ahmad M, Pomerantz RJ, Wigdahl B, Parveen Z (2008) Antiviral potentials of medicinal plants. *Virus Res* 131(2):111–120
- Murdock RT, White GL Jr, Pedersen DM, DeFaller JM, Snyder CC (1990) Prevention and emergency field management of venomous snakebites during military exercises. *Mil Med* 155:587–590
- Nair CKK, Parida DK, Nomura T (2001) Radioprotectors in radiotherapy. *J Radiat Res* 159:812–834
- Puri SC, Nazir A, Chawla R, Arora R, Riyaz-Ul-Hasan S, Amna T, Ahmed B, Verma V, Singh S, Sagar R, Sharma A, Kumar R, Sharma RK, Qazi GN (2006) The endophytic fungus *Trametes hirsuta* as a novel alternative source of podophyllotoxin and related aryl tetralin lignans. *J Biotechnol* 122(4):494–510. Epub 2005 Dec 20
- Rathor R, Sharma P, Suryakumar G, Ganju L (2015) A pharmacological investigation of *Hippophae salicifolia* (HS) and *Hippophae rhamnoides turkestanica* (HRT) against multiple stress (C-H-R): an experimental study using rat model. *Cell Stress Chaperones* 20(5):821–831. <https://doi.org/10.1007/s12192-015-0603-2>. Epub 2015 Jun 5
- Rider TH, Zook CE, Boettcher TL, Wick ST, Pancoast JS, Zusman BD (2011) Broad-spectrum antiviral therapeutics. *PLoS One* 6(7):e22572
- Sagar RK, Chawla R, Arora R, Singh S, Krishna B, Sharma RK, Puri SC, Singh P, Kumar R, Sharma AK, Singh S, Prasad J, Gupta V, Ahmed B, Dhar KL, Khan HA, Gupta ML, Qazi GN (2006) Protection of the hemopoietic system by *Podophyllum hexandrum* against gamma radiation-induced damage. *Planta Med* 72(2):114–120

- Sharma P, Suryakumar G, Singh V, Misra K, Singh SB (2015) In vitro antioxidant profiling of sea buckthorn varieties and their adaptogenic response to high altitude-induced stress. *Int J Biometeorol* 59(8):1115–1126. <https://doi.org/10.1007/s00484-014-0925-2>. Epub 2014 Nov 11
- Singh J, Shah NC (1994) *Podophyllum*: a review. *Curr Res Med Arom Plant* 16:53–83
- Singh J, Bhoi S, Gupta V, Goel A (2008) Clinical profile of venomous snake bites in north Indian Military Hospital. *J Emerg Trauma Shock* 1(2):78–80
- Singh PK, Kumar R, Sharma A, Arora R, Chawla R, Jain SK, Sharma RK (2009a) *Podophyllum hexandrum* fraction (REC-2006) shows higher radioprotective efficacy in the p53-carrying hepatoma cell line: a role of cell cycle regulatory proteins. *Integr Cancer Ther* 8(3):261–272
- Singh PK, Kumar R, Sharma A, Arora R, Jain SK, Sharma RK (2009b) Pifithrin-alpha decreases the radioprotective efficacy of a *Podophyllum hexandrum* Himalayan mayapple fraction REC-2006 in HepG2 cells. *Biotechnol Appl Biochem* 54(1):53–64. <https://doi.org/10.1042/BA20080250>
- Srivastava KK et al. (1996) Studies on combat Stress, Physiological, Biochemical and Physiological correlates. DIPAS ReportNo 11/96
- Swaroop A, Sinha AK, Chawla R, Arora R, Sharma RK, Kumar JK (2005) Isolation and characterization of 1,3-dicapryloyl-2-linoleoylglycerol: a novel triglyceride from berries of *Hippophae rhamnoides*. *Chem Pharm Bull* 53(8):1021–1024
- Swaroop A, Sinha AK, Chawla R, Singh S, Sagar RK, Sharma RK, Kumar R, Sharma A, Gupta ML, Singh S, Prasad J, Khan HA, Swaroop A, Sinha AK, Gupta AK, Tripathi RP, Ahuja PS (2007) Radioprotective and antioxidant activity of fractionated extracts of berries of *Hippophae rhamnoides*. *J Med Food* 10(1):101–109
- Thakur P, Chawla R, Chakotiya AS, Tanwar A, Goel R, Narula A, Arora R, Sharma RK (2016) *Camellia sinensis* ameliorates the efficacy of last line antibiotics against carbapenem resistant *Escherichia coli*. *Phytother Res* 30(2):314–322
- Tanwar A, Chawla R, Ansari MM, Thakur P, Chakotiya AS, Goel R, Ojha H, Asif M, Basu M, Arora R, Khan HA (2017a) In vivo anti-arthritis efficacy of *Camellia sinensis* (L.) in collagen induced arthritis model. *Biomed Pharmacother* 87:92–101
- Tanwar A, Thakur P, Chawla R, Ansari MM, Chakotiya AS, Gusain S, Goel R, Arora R, Sharma RK, Khan HA (2017b) Curative remedies for rheumatoid arthritis: herbal informatics approach for rational based selection of natural plant products. NISCAIR-CSIR, New Delhi
- Thakur P, Chawla R, Chakotiya AS, Tanwar A, Goel R, Narula A, Arora R, Sharma RK (2016a) *Camellia sinensis* Ameliorates the efficacy of last line antibiotics against carbapenem resistant *Escherichia coli*. *Phytother Res* 30(2):314–322. <https://doi.org/10.1002/ptr.5535>. Epub 2015 Dec 1
- Thakur P, Chawla R, Tanwar A, Chakotiya AS, Narula A, Goel R, Arora R, Sharma RK (2016b) Attenuation of adhesion, quorum sensing and biofilm mediated virulence of carbapenem resistant *Escherichia coli* by selected natural plant products. *Microb Pathog* 92:76–85. <https://doi.org/10.1016/j.micpath.2016.01.001>. Epub 2016 Jan 11
- Vasin MV (1999) Classification of radiation protective agents as a basis of modern radiation pharmacology. *Radiats Biol Radioecol* 39:212–222
- Vijayaraghavan R, Gautam A, Kumar O, Pant SC, Sharma M, Singh S, Kumar HT, Singh AK, Nivsarkar M, Kaushik MP, Sawhney RC, Chaurasia OP, Prasad GB (2006 Oct) Protective effect of ethanolic and water extracts of sea buckthorn (*Hippophae rhamnoides* L.) against the toxic effects of mustard gas. *Indian J Exp Biol* 44(10):821–831
- Yashavardhan MH, Shukla SK, Srivastava NN, Suar M, Dutta S, Kalita B, Ranjan R, Singh A, Bajaj S, Gupta ML (2016) γ H2AX formation kinetics in PBMCs of rabbits exposed to acute and fractionated radiation and attenuation of focus frequency through preadministration of a combination of podophyllotoxin and rutin hydrate. *Environ Mol Mutagen* 57(6):455–468