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REVIEW PAPER

Biotechnology in Defence

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ABSTRACT

Biotechnology, in its present perspective, encompasses activities, such as recombination of genes; cloning, or making genetically identical copies of a living thing; and splicing of genes from DNA of one organism into the genome of unrelated species, to create new, self-reproducing forms of life. The vast potential of biotechnology is being increasingly realised, and efforts are in progress to harness it for improving quality and quantity of bio-weapons. The bio-weapons, as such, are highly attractive because of their non-detection by routine security systems, ease of access, low production cost and easy transportation. A wide range of genetically manipulated organisms and their by-products are considered to have an added advantage, because these genetically manipulated biologics not only accentuate the existing properties of bio-weapons, but also could be made target-specific. Biotechnology, if used prudently, can play a significant role to counter such threats of biologics, viz., by producing (i) bio-armoury comprising powerful antibiotics, antisera toxoids and vaccines to neutralise and eliminate a wide range of diseases, and (ii) bio-sensors for rapid detection, identification and neutralisation of biological warfare agents. This article elucidates some facets of biological warfare, legal protective strategies emphasised through international consultation, cooperation and adherence to the Biological and Toxin Weapons Convention, and discusses how biotechnology could be effectively used to strengthen countries' defence and combat the threat of biological warfare.

Keywords : Biotechnology, bio-weapons, human cloning, biological warfare , chemical warfare, biologics, gene slicing, genomics, genetic engineering, biological weapons, bio-armoury, bio-sensors, recombinants DNA technology

1. INTRODUCTION

The term biotechnology was originally coined to explain the commercial use of living organisms. However, with increase in information on deoxyribonucleic acid (DNA) and advent of recombinant DNA technology, all activities associated with gene manipulation (genetic engineering) have also been included in the domains of biotechnology. Today, biotechnology is a multidisciplinary science, and, by virtue of its vast potential, has influenced all walks of life, viz., food, fodder, agriculture, sericulture, biopolymers, industry, medicine, warfare, and as a consequence, national defence programme. Biotechnology/genetic engineering often makes use of artificially constructed vectors to carry genes to multiply unlimited copies of genes, and also to insert genes into cells. Once inside cells, these vectors slot themselves into the host genome, resulting in transgenic organisms carrying desired transgenes. Using an appropriate combination of vectors, genes and hosts, a large number of genetically engineered products, such as rapeseed oil, soybean, maize, sugarbeet, squash, cucumber, BST-milk and tomatoes, are already available in the market, or are soon to arrive. Transgenic animals (mice) are increasingly being used in laboratories for experimental work.

While biotechnological progress is on to meet

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the needs of growing population, there are increasing global speculations about the misuse of such a technology and genetically engineered material, particularly to strengthen the warfare programmes[1]. It is opined that biotechnology could lead to disasters far worse than those caused by accidents in nuclear installations because genes can replicate, spread and recombine indefinitely. Cloning of *Dolly* is being visualised as an advancement just short of human cloning, and has already triggered worldwide debate on the ethics of such experiments, their uses and necessity. In June 1997, President Clinton imposed a five-year ban on human cloning in USA, while the UK House of Commons Science and Technology Committee (STC) wants British law to be amended to ensure that human cloning is illegal[2]. The Science and Technology Committee (UK), French President, Chirac, and German Research Minister, Juergen Ruettgers, are also calling for an international ban on human cloning. Since genetic engineering can boost 'horizontal gene transfer', i.e., the transfer of genes to unrelated species, it may be used to create new pathogenic bacteria and antibiotic resistance among pathogens. It is reported that such horizontal gene transfers are already occurring due to improper handling, storage and disposal of genetically engineered material. It has been alleged that previously unknown bacterial strains responsible for cholera outbreak in India in 1992, and *Streptococcus* epidemic in Tayside in 1991, and *E.coli* (157 strain) outbreaks in Scotland, were the result of genetic recombination subsequent to horizontal gene transfer[3]. According to a 1996 World Health Organisation (WHO) report, at least 30 new diseases, including AIDS, Ebola and Hepatitis C, have emerged over the last two decades. Genes for antibiotic resistance are also believed to have spread horizontally, recombined with one another to generate multiple antibiotic resistances throughout the bacterial population. Practically, all the pathogens identified as responsible for fresh outbreaks of *E. coli,* streptococcal infections and meningitis are reported to be resistant to multiple antibiotics. Two strains of *E. coli* isolated in a transplant ward outside Cambridge in 1993 were found to be resistant to 21 out of 22 common antibiotics[3]. Such microbes are cause of concern because infections with these and other similar strains will not respond to the known treatments, and therefore accidental or intentional release of such genetically engineered organisms into the environment may be disastrous.

Realising the implications of biotechnology in warfare, increasing number of countries are venturing into the development of such programme[4] (from about four in the mid-1970s to about 17 in 1997). Use of bio-weapons in the 1991 Gulf war raises current concerns, and biotechnology has become a prime target of UN regulations. Besides, Biological and Toxin Weapons Convention (BTWC) has been active during the last two-and-half decades in developing international agreements for worldwide prevention of research and development on BTW and disarmament of BTW in countries that were reported to develop and stockpile BTW[5]. The following sections elucidate some aspects of biological warfare and how biotechnology can be exploited to strengthen the defence programme.

2. BIOLOGICAL WARFARE & BIOTECHNOLOGY

Biological warfare is the use of disease-producing agents to harm or kill adversary's military forces, population, food, and livestock. This includes any living (or non-living virus) microorganism or bio-active substance that can be delivered by conventional warhead or using civilian means. An attack with bio-weapons using antibiotic-resistant strains could initiate the occurrence and spread of communicable diseases, such as anthrax and plague, on an endemic or epidemic scale. Deliberate contamination of food with herbicide, pesticide or a heavy metal results in food insecurity. Intentional release of pathogenic organisms that kill cash crops and destroy the reserves of an enemy constitute a powerful weapon of biological warfare and bioterrorism. Anti-crop warfare involves use of biological agents and herbicides, which cause debilitating famine, malnutrition, decline of agriculture-based economies, and food insecurity. Defoliants in the Vietnam war were widely used as agents of anti-crop warfare targeted at sweet potatoes, soybeans, sugarbeets, cotton, wheat, and rice[4] .

Though the evil idea of biological warfare existed from ancient times, the advent and progress of biotechnology has made biological warfare more complex. Today, many developing countries visualise biological weapons to be of two-fold utility, (i) as 'a poor man's atomic bomb', intended to deter attacks from stronger, unconventionally armed neighbours; and (ii) as a relatively cheap force multiplier that can help compensate for shortcomings in conventional arsenals. Because much of the same biotechnology equipment employed by modern pharmaceutical programme or laboratories associated with modern hospitals can be used to foster a biological weapons programmes, identification of an offensive biological warfare programme can be extremely difficult. Most equipment used in biological warfare-related programmes have legitimate applications, providing potential users, the ability to conceal biological weapons activity within the framework of legitimate research and development, and industrial programme. To exemplify, manufacture of vaccines for human or veterinary use can camouflage the production of large quantities of biological warfare agents[6]. Biotechnology, in short, has made the biological warfare-related programmes more complex, target -oriented and ineffectual to verification procedures.

3. EVOLUTION OF BIOLOGICAL WARFARE & ITS PRESENT-DAY SCENARIO

The history of biological weapons and warfare has appeared in a number of reports[7,8]. The first recorded use of biological agents, according to most of the accounts, was by Romans, who used dead animals to foul the enemy's water supply so as to decrease enemy numbers and their morale by spreading disease. The Tartars tried to infect the enemy by catapulting bodies infected with bubonic plague over the walls of the city of Kaffa.

The modern history of biological warfare perhaps started with the thought: 'Science and technology are the keys to winning war and the biotechnology war is the most cost-effective'. Some of the documented events towards biological warfare programmes of a few prominent countries are presented below:

In 1918, a special section of the Army in Japan (Unit 731) dedicated to biological warfare was constituted which conquered a large part of Manchuria and all prisoners of war were exploited for biological warfare experiments.

Then, in 1941, the US became aware of the Japanese efforts and decided to start its own biological warfare programme. Most of the offensive tests at that time were based on secret spraying of organisms over populated areas which were later shut down. One of their biggest experiments involved use of *Serratia marcescens* being sprayed over San Francisco. At one point, 5000 particles/min were sprayed from the coastal areas inward. In hindsight, now that some of this information has become declassified, it has been shown that during the periods following spraying tests, normal infections increased by 5-10 times[9].

Around the same time, the UK was also developing a programme in biological warfare, focused on anthrax spores, their viability and range of spread. The Gruinard island off the coast of Scotland was chosen as the site for this testing since it was far off the coast. This distance was considered sufficient to prevent contamination of the mainland, which later turned out to be false and outbreak of anthrax in sheep and cattle was experienced in 1943 on the coast of Scotland that directly faced Gruinard; and even till today, Gruinard island is contaminated with *Bacillus anthracis* spores. Decontamination by brushfire burned off the top of the soil and killed all traces of the organisms, but spores embedded in soil prevented total decontamination of the island. This island is a threat till date because, as long as no ground is disturbed, it is assumed that one is safe, but birds that travel back and forth from mainland to island could become one of the carriers and consequences could be enormous[10].

The current status of biological weapons and warfare is tenuous. There is a general agreement among many countries that biological weapon is inhumane and that it should not be used for first strike, retaliation of kind, or defensive purposes. This thought is, however, not universally shared, and many less-developed countries see biologics as an easy and less expensive way to possess weapons of mass destruction.

4. BIOTECHNOLOGICALLY EVOLVED BIOLOGICAL WEAPONS

Biological weapons can be classified into viruses, bacteria, rickettsiae, biological toxins[11,12] (Table 1), and then genetically altered organisms. The genetically altered organisms would usually be some kind of mutant of the existing microorganisms expectedly more virulent and/or less susceptible to known treatments. Any toxin or substance, created or acquired through recombinant technology, falls into this class as well and could be some kind of fused protein (antibody and/or toxin) which may be person-specific or group-specific.

Besides the organisms listed in Table 1, there are other microorganisms also considered as a threat, viz., *Ebola* virus, *Hanta* virus; bacteria, such as *Vibrio cholerae, Salmonella typhi, Staphylococcus aurous* and *Rickettsia prowasecki*. The details of usage of these microorganisms at warfare level are, however, not available.

5. BIOTECHNOLOGICALLY EVOLVED BIOLOGICAL WEAPONS: PROS & CONS

There are a number of advantages and disadvantages of biotechnologically evolved biological weapons. Probably the biggest advantage is relatively high killing efficiency of most biological weapons. It is estimated that 1 g of toxin could kill 10 million people. A purified form of *botulinum* toxin is approx. 3 million times more potent than sarin, a chemical nerve agent. As a comparison, a Scud missile filled with *botulinum* toxin could affect an area of 3700 km^2, an area 16 times greater than could be affected with sarin. Another advantage is the cost-effectiveness of biological weapons. To affect 1 km^2, it would cost approx. $2000 using conventional weapons, $800 using nuclear weapons, $600 using chemical weapons, and $1 using biological weapons[13,14]. In a televised address in November 1997, while holding up a 2.265 kg bag of sugar, US Defence Secretary, William S. Cohen pronounced that an equivalent amount of anthrax, if properly dispersed, could kill half the population in Washington, D.C. Another Defence Department warning stated that only 9.060 kg of anthrax, sprayed from the back of a truck moving down Broadway in Manhattan, could kill up to 1.8 million people[15]. This fact has made biological warfare agents to be called a poor man's atomic bomb. Any nation with a reasonably advanced pharmaceutical and medical industry has the capability of mass production of biological warfare agents. Another advantage of biological weapon is that anything from a piece of fruit to a ballistic missile could be used to deliver a biological weapon to a target. Along with this is the fact that, with certain organisms, only a few particles would be needed to start an infection that could potentially cause an epidemic. Whereas conventional weapons explode once and are finished, a few particles of *Hanta* virus may infect and kill thousands of people and still continue to infect population for several generations *via* the carriers[16].

The disadvantages of biological weapons are many, but a major consideration is unpredictability of their use. Weather is an important consideration, and Gruinard island is a prime example of how uncontrolled spread could leave entire mankind helpless. The life-span of agents is another major concern, because these agents are living creatures and have a chance of becoming a part of local micro-flora. This may make the entire area uninhabitable even after the organism is killed. The last major disadvantage of biological weapon is the stigma associated with its use. A ruler of a country, accused of purposely harming mankind for several generations, just for military gains, is not likely to be pardoned for ages[17].

6. BIOTECHNOLOGY & DEFENCE PROGRAMMES

The Geneva Protocol of 1925 first banned the use of chemical and biological weapons, but it was silent on the development of these weapons. Although, in 1972, the BTWC was framed, which was ratified by approx. 150 nations, other confidence-building measures are also required to combat the threat of biological weapons[18,19]. Review conferences that are held under the auspices of the UN on a nominal five-year cycle, is another such step. According to an analysis presented by M.I. Cherries and I.Hunger at the International Conference on Peaceful Use of Biotechnology and the Convention of Biological Weapons in 1997, only 26 states provided information

Table1. Some of the microbes enlisted as bio-weapons

Type of agent	Name of agent	Rate of action	Effective dosage	Symptoms/effects
Bacteria	*Bacillus anthracis* (causes anthrax)	Incubation: 1-6 days Length of illness: 3-5 days	10,000 spores or less	Fever and fatigue; often followed by a slight improvement, then abrupt onset of severe respiratory problems; shock; pneumonia and death within 2-3 days
	Yersinia pestis (causes bubonic plague)	Incubation : 2-10 days Length of illness: 1-2 days	100-20,000 organisms	Malaise, high fever, tender lymph nodes; can lead to hemorrhage, circulatory failure, and death
	Brucella suis (causes brucellosis)	Incubation: 1-3 weeks Length of illness:	1,300 organisms	Fever and chills, headache, loss of appetite, mental depression, extreme fatigue, aching joints and sweating
	Pasteurella tubarensis (causes tularemia)	Incubation:3-5 days Length of illness: 30-60 per cent victims die within 30 days	10-50 organisms	General pain, an irritant, cough, feeling of general illness
Rickettsiae	*Coxiella burnetii* (causes Q-fever)	Incubation: 10-20 days Length of illness: 2 days–2 weeks	10 or less organisms	Pneumonia, cough, chest pain
Viruses	*Venezuelan equine encephalitis*	Incubation: 1-5 days Length of illness: Days to weeks	25 infectious units	Fever, chills, gastrointestinal hemorrhage, severe headache, nausea, vomiting, delirium;can lead to coma, shock, and death
Toxins	Saxitoxin	Time to effect: Minutes to hours Length of illness: Fatal after inhalation of lethal dose	150 μ g	Dizziness, paralysis of muscles of respiration; death within minutes
	Botulinum toxin	Time to effect: Hours to days Length of illness:24-72 hr	70 n g	Weakness, dizziness, dry throat and mouth, blurred vision, progressive weakness of muscles; abrupt respiratory failure may cause death
	Ricin	Time to effect: Hours Length of illness: 7-10 days	200 μ g	Rapid onset of nausea, vomiting, severe cramps, vascular collapse; can start with non-specific symptoms of weakness, fever, and cough
	Staphylococcus enterotoxin B	Time to effect: A few hours Length of illness:4-6 days	2,000 μ g	Severe nausea, diarrhea, and vomiting

Use of Biotechnology and the Convention of Biological Weapons in 1997, only 26 states provided information on their defencive programmes between 1992-97, and 17 of these states declared such programmes to be active[20].

It is reported that since mid-1980 the attention of military intelligence has been altered towards harnessing genetic engineering and recombinant DNA technology for updating and devising lethal weapons and also developing stragies to combat the threat from such genetically engineered weapons[21].

Larger volumes of funds have been sanctioned[22] for research on:

- Vaccines against a variety of bacteria and viruses identified in core control and warning lists of agents used for biological warfare.
- Rapid detection, identification and neutralisation of biological and chemical warfare agents.
- Development of deterrents, viz., genetically modified organisms, bio-weapons with either incapacitating or anti-animal agents, eg, rabbit calcivirus disease (RCD), anti-plant contagious agents of rust, smut, etc.

Bio-catalysis has emerged as a viable technique for the detection and/or detoxification of organo-phosphorus neurotoxins and their derivatives[23]. Efforts at global level are in progress to enhance catalytic lifetimes, environmental sensitivity and general applicability, devising of enzyme-based reusable sensors for the detection of anti-human biological agents, nerve agents and the precursors that are used in the synthesis of the same.

7. CONCLUSION

The use of biological weapons has a long and varied history. Interestingly enough, its use has decreased as history has progressed, instead of proliferating, like most kinds of warfare. The development of biotechnology has opened new doors for the use of biological weapons and it remains to be seen where we will go with it. There are efforts to have a global ban on all kinds of biological and chemical warfare agents, but no one can predict how these will turn out or how well they will work.

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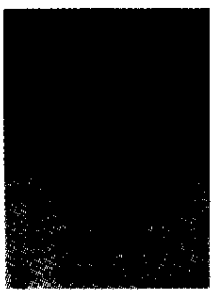

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