

Editorial

LIMITATIONS OF THE CONTEMPORARY VACCINES: HOW TO OVERCOME ?

Shibabrata Pattanayak*

ABSTRACT: Vaccines are used generally to prevent a few infectious diseases by stimulating the weapons of acquired immunity of the body against specific antigens. Along with desired antigens or their source, many other assisting materials are added to the vaccines. There are reports of failure of vaccination as well as of some instant side effects possibly due to the ingredients used in the vaccines. Many important infectious diseases are not covered by vaccination due to various reasons. The non-specific immunity power of the body can be modulated to prevent both infectious diseases as well as diseases of other origins. Following a designed lifestyle and intake of succulent biomedicines can be the two arms for achieving the target. The succulent biomedicines can also supply different important micronutrients and nutraceuticals to the body and also can incur many positive effects on different body systems by the activities of the phyto-constituents individually, as well as through their combinational effects.

Keywords: : Acquired immunity, Vaccination, Limitation, Innate immunity, Succulent biomedicines, Lifestyle modification.

Vaccines are produced artificially and used to initiate or strengthen the immune response against diseases in the body. So, these can assist in developing specific immunity against some specific pathogens. Most of the vaccines are used as an injectable item for apparently healthy humans or animals and only a few are advocated for oral intake. The majority of vaccines require repetition after a few months or years to develop or to keep the protective immunity power of the body at the level of prevention of diseases. Vaccinations mimic the natural way for the development of active immunity against any disease-producing organism following the recovery from clinical or subclinical infection of the organism [1, 2].

The development of protective antibodies against the disease of interest inside the body is the main target of vaccination. These antibodies can act against the specific disease-producing organisms (or proteins in some cases) in the body. So, generally, vaccination is performed for disease specifically, and thus vaccination against one disease cannot protect the vaccinated individuals from other diseases. A large portion of human diseases (60-75%) are derived from

non-human species (zoonotic spillover) and the trend shows that the deaths due to such diseases may increase 12 times in 2050 in comparison to 2020 [3, 4]. So, the scope of prevention of infection of various types of disease-producing organisms (maybe a few thousand) is not possible by performing vaccination against all of them.

Along with that limitation, there may be some other undesirable effects of the presently used vaccines. Various parameters of contemporary vaccines are discussed and a possible adjunct or alternate way of vaccination to strengthen the disease-preventive power of the body is searched out in this article.

CONTEMPORARY VACCINES: TYPE AND COMPOSITION

A. Types of vaccine

The main types of vaccines currently in use are inactivated vaccines, live-attenuated vaccines, mRNA vaccines, recombinant vaccines, subunit vaccines, conjugate vaccines, polysaccharide vaccines, viral vector vaccines, and toxoid vaccines [1, 5, 6].

Editor, Exploratory Animal and Medical Research.

*Corresponding author. e-mail: pattanayak1966@gmail.com

Limitations of the contemporary vaccines : how to overcome ?

B. Composition of vaccines

Along with antigens or resources capable of supplying antigens, many other materials are added during the preparation of a vaccine. The addition of such chemicals varies from vaccine to vaccine. A description of some of such components is available in the literature.

1. Active component - the antigen or materials supplying antigen.

These may be of different types, like attenuated live viruses, inactivated viruses or bacterium, part of the virus or bacterium, part of toxin produced by the bacterium, etc.

2. Adjuvant: These chemicals are added to the vaccines to enhance the immune response of the body to the vaccine antigen. Various aluminum salts [as aluminum hydroxide, aluminum phosphate, potassium aluminum sulfate (alum), etc.] are commonly used for that purpose. Other materials, like oil in emulsion (as MF 59, AF03, or AS03 using squalene) [7], part of other organisms (as AS04 contains modified molecules from the *Salmonella minnesota* bacterium) [8], etc. are examples.

3. Stabilizers: Sugars like sucrose and lactose, amino acid glycine, monosodium glutamate, serum or recombinant albumin (bovine or human origin), gelatin (partially hydrolyzed collagen of porcine or bovine origin), etc.

4. Preservatives: Thiomersal (a mercury-containing compound), 2-phenoxyethanol (aromatic ether alcohol), phenol (carbolic acid), etc.

5. Buffers: Buffers are used to control the changes in pH, maintain osmolarity and adjust tonicity. Sodium chloride is used generally for that purpose.

6. Surfactants: These are used to keep particles suspended in liquid vaccines by preventing settling or clumping by reducing the surface tension of the vaccine liquid. Examples are - polysorbate 80 (prepared from sorbitol), oleic acid (omega-9 fatty acid), etc.

7. Solvent: Distilled water is generally used for that purpose.

8. Trace components: Cell culture media fluids and components, egg proteins, yeast, antibiotics (such as

Neomycin, Kanamycin, Streptomycin, etc.), inactivating agents (such as formaldehyde), etc. [9, 10].

So, as per the available literature, it appears that we get many compounds of synthetic or semi-synthetic origin along with the vaccine antigen through different vaccines inside our bodies.

HOW VACCINES WORK ?

Vaccines act as immune-modulators inside a living body. They influence the immune system of the body in the work of identification and then combating the infecting enemies by some easier fights. The invading pathogens, mainly some bacteria, and viruses, are prevented in that way. The vaccinal antigens are injected and the body recognizes them as some foreign particle and so deals with them in the same way as they do with invading micro-organisms. Thus, the immune system of the body becomes trained against the invading vaccinal antigen (mimicking the original pathogen) and produces antibodies against them and the character of the enemies is remembered by the cells engaged in this work. In any future infection of such microorganisms (bacteria or viruses), this knowledge of the immune system of the body is utilized and the already sensitized soldiers can perform the work of fighting and eliminating the enemies in a far better way so that they cannot multiply to cause any serious illness [11, 12].

FAILURE AND SIDE EFFECTS OF VACCINES

A. Failure of vaccines

Vaccination failure means the development of a specific disease in a vaccinated individual despite getting the vaccine. Such a condition may develop due to actual failure of the vaccine or due to failure to vaccinate the individual appropriately [5, 13].

Vaccine failure can be divided into two categories.

Primary vaccination failure

When the recipients of a vaccine fail to develop protective antibodies, the condition is termed primary vaccine failure. The main reasons behind such failure are the deficiency in the immunity power of the individuals to show proper response to the vaccines.

Secondary vaccination failure

In that type of vaccine failure, the patients develop a normal immune response after vaccination initially

but fail to prevent disease after getting a natural infection. Usually, the protective effect of most of the vaccines wanes over time, particularly in the absence of boosting doses and the chance of secondary vaccine failure increases over time [13, 14].

B. Factors affecting failure of vaccination

1. Variation in the strain of the organism used in vaccine preparation and the infecting one.
2. Destruction of the protective epitope of the vaccinating antigen during the preparation of the vaccine.
3. Presence of insufficient antigen in the vaccine given to an individual to elicit protective immunity.
4. Damage to the vaccines due to improper storage and transport.
5. Improper administration of the vaccine to the recipients.
6. Presence of maternal antibodies among the children during vaccination.
7. Vaccination performed in the individuals already infected and incubating the disease organism.
8. Individuals less responsive to the vaccines due to genetic makeup, suffering from immunodeficiency diseases (such as AIDS), or due to other reasons.
9. Vaccinated Individuals stay under immunosuppressive medication.
10. Severe malnutrition, high parasitic load, anemia, etc. of the vaccine receptors.
11. Severe stress, staying in extreme heat or cold, fatigue, pregnancy, etc. can cause vaccine failure, which may be due to increased production of glucocorticoids.
12. Vaccination of a very small number of individuals against a widespread disease with high infectivity leads to failure of the development of herd immunity [1, 13, 14].

C. Side effects of vaccines

1. Showing symptoms of mild toxicity by the vaccinated individuals is very common after vaccination. Inflammation, edema, tissue necrosis, etc. near the area of vaccine inoculation are the common problems encountered after vaccination. Symptoms like pyrexia, restriction in limb movement due to pain, anxiety, depression, neurological complication, etc. are also commonly seen.
2. As the inoculated vaccines contain many synthetic and semi-synthetic substances along with antigens, there is always a chance of developing hypersensitivity

reactions against one or more of such items. The severity of the reaction depends on various factors of the vaccinated person (genetic makeup, age, condition of health, etc.).

3. Low-level immune-suppression is common among vaccinated individuals. This may invite some other problems in individuals with some specific continued medication or having some pre-existing health disorders.

4. The stress of the vaccination can activate latent infections among some individuals [14, 15, 16].

5. It is argued that live viral vaccines can cause changes in virulence and species specificity of other related viruses after reaching the biosphere and can initiate rapid spread of some diseases among the population [2].

The identified gross side effects found within a very brief period after vaccinations are documented, but there are many grey areas. Nothing works inside a body system alone. The cumulative effects of vaccine ingredients with other xenobiotic residues, their long-term effects, etc. require vigorous study before coming to any final conclusion.

SUCCULENT BIOMEDICINES - THE WEAPON TO STRENGTHEN INNATE IMMUNITY

Innate immunity and vaccination

The innate or non-specific immunity of the body is considered the first line of defense against all kinds of invasions of the body. The invading components may be of different types - physical, cellular, chemical, biochemical, etc. The innate immunity system covers many preventive measures of the body - from primary barriers like skin, gut, nasal hair, lacrimal gland, etc. to activities of different phagocytic cells, gamma-delta ($\gamma\delta$) T lymphocytes, Natural Killer cells, etc. as well as actions of different cytokines.

So, the arms of the innate immunity system start its action against the invading disease-producing pathogens at the very beginning. After crossing these barriers, an organism can proceed further to create any disease. The fighter cells of the host can recognize the pathogenic organisms by their pattern recognition receptors encoded by their germ-line and then trigger various types of mechanisms to remove those [12, 17].

Limitations of the contemporary vaccines : how to overcome ?

Vaccination acts to modulate body immunity by acting on another arm of the immunity system of the body - the adaptive or acquired immunity system. Generally, vaccines cannot influence innate immunity to any noticeable extent.

A joint venture may be better than single

Modulation of the innate immunity system of the body added with disease-specific modulation of adaptive immunity by use of vaccination may have far more beneficial effects to the body system than the activity of vaccination alone. So, the joint venture of both arms (innate and acquired immunity) can be performed in the cases where vaccination is available or possible. In other cases, modulated innate immunity can be engaged to prevent many other diseases.

The innate immunity modifiers can be principally of two types.

i) Following of designed lifestyle

There are some ways to influence the innate immunity power of the body. Along with correction of wrong food-drink habits (such as the exclusion of processed foods, chemicals, and chemical added drinks, nasty fats, and inclusion of fiber-rich foods, vegetables, fruits, etc. in the diet) and other lifestyle-related factors like a violation of body clock, and inclusion of positive factors like exposure to sunlight, practice of Yoga, ample physical exercise, etc. in the daily routine, the initiation and progression of almost all diseases can be strongly influenced by modulation of the immunity power of the body [18, 19].

ii) Use of succulent biomedicines

There are nearly 1200 identified plants having the power to combat infection of different disease-creating organisms [20, 21, 22]. There are also identified 934 plants with reported anti-cancer efficacies and 205 plants with anti-diabetic activities [19, 28]. There is a report of identified 124 edible succulent fruits, 238 vegetables and others as well as other edible nuts, seeds etc. having the capability to modulate the body immunity. Regular daily intake of fruit salad, vegetable salad and nut mixture and weekly intake of mixture of some spices made by the items selected purposefully from the lists can keep the body immunity at a very good level [12, 18, 28].

Infection and immunity of an individual is not any independent subject; rather related to the status of different health-related parameters. Many plants of these lists of the said articles are found common, so it

is expected that they can be used to prevent or cure of all these diseases singly, or together. Edible capsules of the succulent parts of these medicinal plants can be prepared for their effective use. Production of succulent biomedicine capsules and global transportation of them under the cold chain to the consumer or patients can dramatically change the present scenario of the creation of diseases as well as their costly treatment [28]. The procedures related to the chemical-free production of such succulent biomedicines, their bio-preservation and encapsulation, and global transportation has been discussed in some earlier works [19, 21]. Succulent biomedicines can be prepared to be used as a therapeutic means to combat many other diseases. After performing the adoptive research, these medicines can be used therapeutically [20, 22].

MECHANISM OF ACTIVITY OF SUCCULENT BIOMEDICINES

Only very limited research has been performed to understand the mechanism of activities shown by the succulent parts of the medicinal plants, though the ethnic and rural people use medicinal plant parts at that condition most of the time [23, 24, 25]. The activities shown by succulent edible fruits and nuts may have similarities with succulent biomedicines, at least partially [18, 28].

The contemporary studies performed on the medicinal activities of plants are not efficient enough to disclose the complete medicinal activities of a plant. In most cases, the isolated phyto-constituents are studied, but it is just a partial study of a plant. A single medicinal plant contains thousands of phyto-constituents and all of them work together when used in an unaltered state, *i.e.*, a succulent state. In any other state, at their dry condition or after diluents extraction of the dry parts, only a part of these phyto-constituents are allowed to show their activities. The contemporary medicinal systems, from the traditional systems practiced presently like Ayurveda and allied systems (use dry plant parts directly), Homoeopathy (use an ethanol-extracted section of the dry plant parts generally), the modern medicine (analyze the diluents extracted section of the dried plant parts to get active principles) have limited their study within the dry parts of the medicinal plants. With reduced number, quantity and the changed state (non-natural) of the phyto-constituents available in these plant-derived medicines can never be expected to show the total efficacy of the medicinal plants [20].

The succulent biomedicines express their activities differently than the single or isolated compounds used in modern medicine. The following points may be related to the subject.

1. Most succulent biomedicine contains a good number of important micronutrients. These can act on the modulation of body immunity.

2. Following proper modulation of different arms of non-specific immunity - the weak or overactive immunity status of the body may be corrected.

3. Part or all of the available phyto-chemicals of an effective medicinal plant may have a specific ability to influence related arms of the immune system of the body to combat infective micro-organisms.

4. Rejuvenation of different body systems can be performed by succulent biomedicines that ultimately affect the overall body immunity. This is related to the 'Rasayana' concept of the Indian codified healthcare system, Ayurveda [26].

5. Exhibition of qualities like antioxidation, immuno-modulation, anti-inflammatory, cardiogenic, hepatoprotective, diuretic, anti-asthmatic, hypercholesterolaemic, etc. medicinal activities of various plant parts can modulate the whole immunity system of the body [18].

6. During the phytochemical analysis under modern medicine, it was found that even the dry parts of medicinal plants contain a huge number of medicinally active compounds of different chemical natures. These include flavonoids, polyphenols, carotenoids, ascorbate, curcumin, tocopherol, etc. Almost all of these are having some immunomodulatory power [18, 26].

7. Different phyto-constituents present in the succulent biomedicines can act together, so their collective effects are expressed during their use. In many cases, the isolated phytochemicals show toxicity in the possible therapeutic doses [18, 19, 20]. The NCI Natural Products Repository preserved the aqueous and organic solvent extracts of the dry parts of a huge number of reported medicinal plants (about 80,000) to check their therapeutic efficacy, but only very little success was achieved [29]. It is argued that the study of a section of the phyto-constituents of any medicinal plant is an incomplete idea to understand the actual efficacy of any medicinal plant [12, 20, 21]. Such limitation can be overcome by studying the succulent form of the biomedicines - as there may be in-house suppression of any possible ill-effect of one compound by others as well as potentiation of the positive effects. The presence of a very minute amount of one or more compounds (volatile, present at very low, undetectable amounts) may influence the overall total activity of succulent biomedicine to a large extent [20, 27, 28].

BENEFIT OF USE OF SUCCULENT BIOMEDICINES AS SOME IMMUNO-MODULATOR

1. Unlike vaccines, the effects of these are not confined to preventing only one or a few specific diseases of infective origin. It will boost the innate immunity power that can assist in the prevention of possible infection of all microorganisms.

2. As most of these medicines are recommended for oral or local use, so expected to have nil or negligible side effects. As no synthetic chemicals or animal product is added to these medicines, there is no chance of gathering any toxin in any organ or tissue of the body or initiation of any reaction due to the effect of added ingredients.

3. Most of these medicines are also having positive effects in the protection of other diseases of non-infective origins. These may be very important added effects without any additional intervention.

4. Many succulent biomedicines can act as suppliers of important nutraceuticals. Such additional effects are also very important in consideration to keep the body healthy and disease-free.

CONCLUSION

Along with the rationale use of vaccines to increase disease-specific immunity, the other arm of modulation of immunity of the individuals may be stressed to get further beneficial effects in the prevention of the diseases. For infectious diseases where no vaccination is possible and for all other non-infectious diseases, modulation of innate or non-specific immunity of the individuals may be the main weapon to combat them. Directed modification of lifestyle, food-drink style, intake of selected mixtures of succulent fruits, nuts, and vegetables, as well as the use of succulent biomedicines for prevention and control of diseases, can be the novel way to achieve that target.

REFERENCES

1. Tezard IR. *Veterinary Immunology* (10th edn.). 2018; Elsevier, 3251, Riverport Lane, St. Louis, Missouri 63043.
2. Pattanayak S, Manna S. Attenuated and modified vaccine viruses: do they act as a source of some other viral diseases? *Explor Anim Med Res*. 2023; 13(1), DOI: 10.52635/eamr/13.1.1-7.
3. Ellwanger JH, Chies JAB. Zoonotic spillover: Understanding basic aspects for better prevention. *Genetics Molecular Biol* 2021; 44: 1(Suppl 1), <https://doi.org/10.1590/1678-4685-GMB-2020-0355>.

Limitations of the contemporary vaccines : how to overcome ?

4. Meadows AJ, Stephenson N, Madhav NK, Oppenheim B. Historical trends demonstrate a pattern of increasingly frequent and severe spillover events of high-consequence zoonotic viruses. *BMJ Glob Health* 2023; 8: e012026. DOI:10.1136/bmjgh-2023-012026.
5. Tizard IR. Vaccines for Veterinarians, Chapter 1 - A brief history of veterinary vaccines. 2021; Elsevier. <https://doi.org/10.1016/B978-0-323-68299-2.00010-1>.
6. Smith ER. Different types of vaccine and its characteristics. *J Clin Chem Lab Med*. 2022; 5(11): 1000255.
7. Nguyen-Contant P, Sangster MY, Topham DJ. Squalene-based influenza vaccine adjuvants and their impact on the hemagglutinin-specific B cell response. *Pathogens*. 2021; 10(3), DOI: 10.3390/pathogens10030355.
8. Fox CB, Carter D, Kramer RM, Beckmann AM, Reed SG. Current status of toll-like receptor 4 ligand vaccine adjuvants, (Chapter 6). In: Schijns VEJC, O'Hagan DT, editors. *Immunopotentiators in Modern Vaccines* (2nd edn.), 2017; Academic Press. <https://doi.org/10.1016/B978-0-12-804019-5.00006-2>.
9. NCIRS fact sheet, Vaccine components. National Centre for Immunization, Research and Surveillance. 2013; <https://www.ncirs.org.au/sites/default/files/2018-12/vaccine-components-fact-sheet.pdf>.
10. Vaccine ingredients fact sheet. Immunisation advisory centre, University of Auckland, 2014; 01-11. <http://vicparkmed.co.nz/wp-content/uploads/2014/08/ConcernVaccineIngredients20140522V01Final.pdf>.
11. Dai X, Xiong Y, Li N, Jian C. Vaccine types. In: *Vaccines - the history and future*. Kumar V, (Editor). Intech Open; 2019. Available from: <http://dx.doi.org/10.5772/intechopen.84626>.
12. Pattanayak S. Succulent biomedicines - an effective way of getting protection against diseases through immunomodulation. *Explor Anim Med Res*. 2020; 10(2): 112-123.
13. Heininger U, Bachtiar NS, Bahri P, Dana A, Dodoo A *et al.* (2011) The concept of vaccination failure. *Vaccine*. 2011; 30(7), DOI: 10.1016/j.vaccine.2011.12.048.
14. Tizard IR. Vaccine failure and other adverse events in animals. *MSD Vety Manual*. 2022; <https://www.msdevetmanual.com>.
15. Wiedermann U, Garner-Spitzer E, Wagner A. Primary vaccine failure to routine vaccines: Why and what to do? *Hum Vaccin Immunother*. 2016; 12(1), DOI: 10.1080/21645515.2015.1093263.
16. Speers D. The vaccine non-responder. *Virology*. 2015; 17(2), <http://www.ogmagazine.org.au>.
17. Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL *et al.* *Harrison's principles of internal medicine*. 19 th edn. 2015; McGraw-Hill Education.
18. Pattanayak S. Healthcare system using succulent parts of plants, Volume II: Steps for production and marketing of some selected healthcare products. 2019; ISBN: 978-93-5391-625-1.
19. Pattanayak S. Prevention and control of diabetes by intake of succulent biomedicines and following of designed lifestyle: A ready plan for execution. *Internati J Scientif Res Updates*. 2022; 03(02): 081-103.
20. Pattanayak S. Healthcare system using succulent parts of plants, Volume I: For infectious diseases. 2019; ISBN: 978-93-5346-842-2.
21. Pattanayak S. Anti-COVID-19 biomedicines - A layout proposal for production, storage and transportation. *The Open COVID J*. 2021; DOI: 10.2174/2666958702101010166.
22. Pattanayak S. Alternative to antibiotics from herbal origin - outline of a comprehensive research project. *Current Pharmacogenom Personali Medic*. 2018; 16, DOI: 10.2174/1875692116666180419154033.
23. Panda SP, Ravi Prasad, DebBarman R. Some potential medicinal plants used by the tribals of Angul district, Odisha, India. *Explor Anim Med Res*. 2023; 13(S), DOI: 10.52635/eamr/13(S)71-77.
24. Maity P, Mahakur B. Studies on some American exotic weeds of Paschim Medinipur district of West Bengal, India, and their medicinal uses. *Explor Anim Med Res*. 2023; 13(S), DOI: 10.52635/eamr/13(S)109-118.
25. Das A, Ngente NN, Bhattacharya P, Kar S, Datta BK. An ethnobotanical survey of plants used by the people of the Hmar tribe of Dima Hasao district, Assam, North East India. *Explor Anim Med Res*. 2023; 13(S), DOI: 10.52635/eamr/13(S)141-147.
26. Kumar D, Arya V, Kaur R, Bhat ZA, Gupta VK *et al.* A review of immunomodulators in the Indian traditional healthcare system. *J Microbiol Immunol Infect*. 2012; 45: 165-184.
27. Pattanayak S, Mandal TK, Bandyopadhyay SK. Validation and therapeutic use of succulent plant parts - opening of a new horizon of alternative medicine. *Explor Anim Med Res*. 2016; 6(1): 08-14.
28. Pattanayak S. Anti-cancer plants and their therapeutic use as succulent biomedicine capsules. *Explor Anim Med Res*. 2023; 13(S), DOI: 10.52635/eamr/13(S)01-50.
29. Developmental therapeutics program (DTP) (2021) The NCI Natural Products Repository (2021), Division of cancer treatment and diagnosis, National Cancer Institute, 9609 Medical Center Drive, Bethesda/Rockville, MD20850, United States. <https://dtp.cancer.gov/organization/npb/introduction.htm>.

Cite this article as: Pattanayak S. Limitations of the contemporary vaccines: how to overcome? *Explor Anim Med Res*. 2023; 13(2), DOI: 10.52635/eamr/13.2.140-145.