Available online at www.ijpab.com

DOI: http://dx.doi.org/10.18782/2582-2845.7900

ISSN: 2582 – 2845

Ind. J. Pure App. Biosci. (2019) *7*(6), 29-41

Review Article

Indian Journal of Pure & Applied Biosciences

An Insight Review on Application of Plantibodies

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Received: 8.11.2019 | Revised: 14.12.2019 | Accepted: 20.12.2019

ABSTRACT

A plantibody is an antibody produced by plants that have, as well as the advantage, challenge, and limitation of plantibodies, with animal genes. The term "Plantibodies" was created to describe the products of plants that have been genetically modified to express antibodies and antibody fragments in plants. Productions of plantibodies offer several advantages over other methods of antibody production, such as low cost of production, high yield of antibodies, safe and effective approach and bring the product to the market within a short time. Six plant-derived antibodies have been developed as human therapeutics, two of which have reached phase II clinical trials. Agricultural crops such as tobacco, tomato, potato, soya bean, alfalfa, rice, and wheat are commonly used for the production of plantibodies. These plantibodies are formed by various methods like conventional method, cell tissue culture method, breeding, and sexual crossing, transgenic seeds, targeting and compartmentalizing. Plantibodies are now used for large scale medical and veterinary sectors for the treatment of immune disorders, cancers, inflammatory diseases, for the production of vaccines and also for diagnostic purposes. This review highlights the methods of production and application of plantibodies as well as the various types of pharmaceutical antibodies produced in transgenic plants. Hence, scholars should promote their application and use in the field of human and veterinary medicine.

Keywords: *Antibody; Application; Plantibody; Production; Transgenic plant*

INTRODUCTION

Antibodies, also called immunoglobulins, are a group of complex glycoproteins produced by B-lymphocytes and present in the serum and tissue fluids of vertebrates. They constitute the humoral arm of the adaptive immune system and specifically recognize and bind to target antigens on pathogens or toxins produced by such pathogens. This individual and specific binding activity allows antibodies to be used for a variety of applications, including the diagnosis, prevention, and treatment of disease. Typically, antibodies are composed of a basic unit, comprising two identical 'heavy' polypeptide chains and two identical 'light' polypeptide chains, which is covalently linked together by intermolecular disulfide bonds (Andersen & Krummen, 2002; Oluwayelu & Adebiyi, 2016).

Cite this article: Tilahun, H., Negash, G., & Fesseha, H. (2019). An Insight Review on Application of Plantibodies, *Ind. J. Pure App. Biosci. 7*(6), 29-41. doi: http://dx.doi.org/10.18782/2582-2845.7900

Vaccines are traditionally produced in animals and administered to humans for their therapeutic value. Likewise, various strategies have been developed to exploit plants as bioreactors for the production of pharmaceutical antibodies, to engineer antibody-mediated pathogen resistance or to alter the plant phenotype by immunomodulation (Stoger et al., 2002). Now a day's antibody production in plants has acquired significance as an emerging system for the production of many recombinant proteins that can be used for therapeutic purposes (Raja et al., 2014).

A plantibody is an antibody produced by plants that have been genetically engineered with animal DNA. The term "Plantibodies" was created to describe the products of plants that have been genetically modified to express antibodies and antibody fragments in plants. Although plants do not naturally make antibodies, plantibodies have been shown to function in the same way as normal antibodies. Plants are being used in this technology as antibody factories, using their endomembrane and secretory systems to produce large amounts of clinically viable proteins, which can later be purified from the plant tissue (Jain et al., 2011).

The combination of antibodies and plant engineering, two rapidly advancing technologies, has led to emerging strategies in diversified plant species (Deepali et al., 2016). Although antibodies were first expressed in plants in the mid-1980's, (Steger and Duering) by two German graduate students (During et al, 1990), the first report was published in 1989 (Hiatt et al., 1989). Since then a diverse group of "plantibody" types and forms have been prepared. Originally, foreign antibody genes were introduced into plant cells by non-pathogenic strains of the natural plant pathogen Agrobacterium tumefaciens (Horsch et al., 1985) and regeneration in tissue culture resulted in the recovery of stable transgenic plants (Duering et al., 1990; Deepali et al., 2016).

Nowadays, molecular farming of antibodies using plants becomes commonly applied. In this regard, plants have several potential advantages over other production systems. Most importantly, Production of recombinant proteins in plants and their administration provides an added margin of safety when compared to that produced from transgenic animals (Koprowski, 2005). In addition, the capacity of plant cells to correctly fold and assemble, not only antibody fragments single-chain peptides, but also full-length multimeric proteins, since they have similar pathways of protein synthesis, secretion, folding and post-translational modifications. Plants do not serve as hosts for human pathogens. Therefore, there is increased safety (Raja et al., 2014).

Six plant-derived antibodies have been developed as human therapeutics, two of which have reached phase II clinical trials. One of these is a full-length Immunoglobulin G (IgG) specific for EpCAM (a marker of colorectal cancer) developed as the drug Avicidin by NeoRx and Monsanto. The five remaining antibodies are CaroRx, scFvT84.66, Anti-HSV, 38C13 and PIPP (anti-hCG) (Doran, 1999). Though plantibodies have many advantages in the treatment of different pathologic conditions however, the technology is not well known and practiced in Africa in general and in Ethiopia in particular especially in the veterinary sector. Hence, in this review, the application of plantibodies, the advantage, challenge, and limitation of plantibodies are described.

2. CROPS AND PLANTS USED FOR PLANTIBODY PRODUCTION

A large number of different crops can be used to produce antibodies including tobacco (Nicotiana tabaccum and N. benthamiana), cereals (rice, wheat, maize), legumes (pea, soybean, alfalfa) and fruit and root crops (tomato, potato). Many factors should be considered before choosing the crop variety. Leafy crops like tobacco generally have the greatest biomass yields per hectare, because they can be cropped several times a year. Tomatoes also have high biomass yield, but production costs are increased (Schillberg et al., 2002).

Antibodies expressed in potato tubers and cereal grains are stable at room temperature for months or even years without loss of stability, while tobacco leaves must be dried or frozen prior to transport or storage to maintain the activity of recombinant proteins. However, the extraction of proteins from seeds is more expensive than from watery tissue, such as tomatoes (Stoger et al., 2002).

The presence of toxic metabolites such as alkaloids in tobacco presents a disadvantage, so edible plants lacking such compounds would be preferred expression hosts. Since most pharmaceutical antibodies will be produced by industry, the costs of production and processing in different crops will have to be evaluated very carefully (Fischer et al., 2003).

2.1. Criterion for Selecting Host Plant

Before selecting a plant for the production of plantibodies, some points should be considered. Most importantly they are generalized by five main factors such as the plant should be easily genetically engineered, capable of producing high level of specific proteins, should have a well-established technology for gene transfer and expression, knowledge of agricultural techniques and management, physiology, pest and disease of crop/ plant selected should be known and the hosts plants should have no toxic or side effects on the animal body (Poonam et al., 2018).

2.2. Sources of Transgenic Plants

Tobacco: - Tobacco, among leafy crops, has the greatest biomass yield per hectare and allows rapid scale-up because it can crop several times in a year (Fischer et al., 2003). Tobacco grows quickly and has been shown to produce a comparatively large quantity of antibodies. Additionally, tobacco is a non-food/non-feed crop if grown separately; there is less chance of cross-contamination food chain by pharmaceuticals (Schillberg et al., 2002). However, the presence of toxic metabolites is hindrance for its use (Poonam et al., 2018).

Alfalfa and other legumes: - Alfalfa and soya bean are another leafy crop used to produce recombinant antibodies. Alfalfa is a perennial crop that can propagate easily and also have good biomass yield (Bardor et al., 2003). One of the potential advantages of alfalfa is that recombinant antibodies produced as a single glycoform rather than a heterogeneous collection of different glycoforms that are found in other plant systems. Pea, a grain legume also a useful production crop, the reason for its high protein content of the seed. Although at present only low yield is possible with this species (Perrin et al., 2000).

Cereals, Seeds, and Tubers: - Cereals, seeds, and tubers are better sources of plantibodies when we are mainly targeted for long term storage. They can be stored at room temperature and are easily transportable. The most commonly used cereals are rice, wheat, and maize along with legumes such as pea, and soya bean (Schillberg et al., 2002).

Antibodies expressed in potato tubers and other cereal grains are stable at room temperature from months to years together, while tobacco leaves must be dried or frozen for long term storage. However, the extraction of proteins from seeds is more expensive than watery tissue, such as tomatoes (Fischer et al., 2003).

Fruits and Vegetables: - Fruits and vegetables can be consumed raw or as partially processed material, which makes them suitable for passive oral immune therapy. E.g. Tomatoes, bananas, Potato, etc. Tomatoes have outstanding properties for pharmaceutical protein production, such as high biomass yield and the advantage of contained growth in the greenhouse. Hence, tomatoes were first used to produce a plant-derived rabies vaccine (Stoger et al., 2000).

Potato has been used widely for the production of plant-derived vaccines and been administered to humans in most of the clinical trials so far (Prasad et al., 2017). Transgenic tomato-based developed edible vaccine expressed cholera toxin B against cholera in the ripening tomato fruit under the control of tomato fruit-specific E8 promoter using Agrobacterium-mediated transformation (Jiang et al., 2007).

3. PURIFICATION AND TECHNIQUE OF PRODUCTION OF PLANTIBODIES

3.1. Purification

The main reason for raising antibodies in plants is its easy purification and low downstream processing. Easy Purification of plantibodies makes biopharmaceutical production more economic (Arntzen, 1998). Transgenic seeds assure excellent storage properties and thus added flexibility in processing management and batch production. Separation of plantibody in seeds is less complicated because of the limited range of endogenous proteins (Kusnadi et al., 1997).

Efficient purification procedures for plant production systems are as important as effective expression levels. In a plant expression system, the plant tissue and cells should be disrupted to release antibodies for purification since the antibody is expressed and localized within the cells. In addition, antibodies should be recovered with the removal of cell debris, noxious chemicals, and contaminants (Valdes et al., 2003).

Although several affinity tagging systems such as the histine tag and intein fusion expression have been applied for purification of recombinant proteins, these systems do not resolve the problems caused by plant cell debris. Therefore, oleaginous plants such as rapeseed oil are useful hosts for monoclonal antibody (mAb) production and purification since the oil bodies can be applied to simplify the first steps of antibody isolation (Seon et al., 2002).

The absence of human pathogens in plants eliminates expensive validation of virus removal steps during purification. But the probability of presence of a diverse burden on plants grown outdoors in non-sterile conditions is high. So, the process for elimination or minimization of contamination with endotoxin and mycotoxins will be necessary in all commercial processes to purify antibodies. Phenolics can interact with proteins in ways that can irreversibly alter the properties of proteins but most of the phenolics released during extraction are small in size, water-soluble, and removable by ultrafiltration steps (Gegenheimer, 1990; Priya et al., 2011).

Alternative methods including the use of oleosin- or polymer-fusions to facilitate purification of recombinant proteins have been discussed and may also be applicable to antibody molecules (Daniell et al., 2001). The main techniques used for the purification of plantibodies are filtration, immunofluorescence, chromatography, defiltration, polymer fusion and protein A-sepharose chromatography. Some other techniques such as RIA (Radioimmunoassay), northern blot technique, ELISA (Enzyme-linked immune sorbent assay), western blot analysis and immunofluorescence southern blot analysis have been used of evaluation of plantibody (Prasad et al., 2017).

3.2. Methods for Plantibody Production

Various techniques have been developed to exploit plants as bioreactors for the production of pharmaceutical antibodies (Prasad et al., 2017).

3.2.1. Conventional method

It uses stable transformation and transient expression to introduce new genes into a host cell. Once the desired DNA from the transformed host cell is isolated and purified, it can be injected into the embryo of a maturing plant, which we want to use for plantibodies production. After injecting the desired gene, followed by the propagation of plants in open fields allow large scale production of plantibodies (Moffat, 1989). However, purification of these proteins is long and tedious, since, upon isolation of the antibody, several proteins, organic molecules glycans, and herbicides must also be isolated, leading to a complex purification process (Kusnadi et al., 1997).

3.2.2. In vitro cell and tissue cultures

This is an economically important method for producing plantibodies wherein plant cells in differentiated stages are grown under controlled conditions having desired genes/ proteins and are harvested either in the form of biomass and culture liquid or combination of both. This method offers large amounts of

recombinant proteins produced in a shorter time (Doran, 1999).

This method has many advantages over the conventional method of plantibodies production by overcoming the problem of extracting and purifying proteins but this method has not used for edible vaccine production. In this method, no sexual reproduction is needed, so transgenic stability is increased because of the absence of crossing over, segregation and recombination and provides more chances in plantibodies production (Ferrante & David, 2001).

3.2.3. Breeding and sexual crossing

This method involves transformation to introduce kappa chains of either light or heavy chains into the host plant. The same is done with gamma chains of either light or heavy regions. Upon crossing one plant with kappa chains and another plant with gamma chains, an antibody is produced which expresses both chains (Jain et al., 2011). This method provides an easy way to produce plantibodies without the need for double fertilization (Ferrante & David, 2001).

3.2.4. Transgenic seeds

Some researchers suggest the use of transgenic seeds in place of green plant tissue for the production of plantibodies as green plants cannot store antibodies for a long period of time. This is because they contain proteases that degrade the recombinant protein. Thus, transgenic seeds can store antibodies for an extended period without degradation because they contain a low level of proteases (Oluwayelu & Adebiyi, 2016).

3.2.5. Targeting and compartmentalization

Targeting signals can be used to retain recombinant proteins within different compartments of the cells such as endoplasmic reticulum, chloroplasts, intracellular space, etc. This is done to preserve the integrity, protect them from proteolytic degradation and to increase accumulation levels of the recombinant protein. This is achieved by tagging the antibodies with a small peptide sequence which can be targeted to a specific compartment of the cell (Jain et al., 2011).

4. APPLICATION OF PLANTIBODIES

The use of transgenic plants for the expression of molecules with therapeutic, diagnostic or veterinary applications has been documented in the last decade. The applications are increasing because recombinant DNA is very useful in creating proteins that are identical when exposed to a plant's (Ayala et al., 2009). This technology represents a great opportunity for the pharmaceutical industry since biological products now account for a large percentage of all pharmaceutical compounds. Several plant-produced antibodies are presently undergoing clinical trials (Oluwayelu & Adebiyi, 2016).

4.1. Therapeutic Applications

Therapeutic applications of plantibody are the treatment of infectious disease, inflammation, autoimmune disease or cancer. Tobacco produced mAb is a more viable alternative to mAb produced in mouse ascites fluid for the large amounts needed for the purification of the hepatitis B vaccine. Plant produced antibodies have also been investigated for inflammatory disease and to induce tolerance (Prasad et al., 2017).

A caries vaccine the first clinically tested plantibody produced in the world that prevent and protects against tooth decay. Streptococcus mutans has been identified as the major etiological agent of human dental caries. The development of a vaccine for tooth decay has been under investigation for more than 30 years. Planet Biotechnology developed a monoclonal antibody against S. mutans, branded CaroRx, produced with transgenic tobacco plants. It is the first plant-derived antibody created from tobacco (Fischer et al., 2006).

CaroRx is a Sig A secretory antibody. It is a clinically advanced anti Streptococcus mutans secretory immunoglobulin, a plantibody that binds specifically to the bacterium, thus protecting humans from dental carries (Larrick et al., 2001). CaroRx® has been used in human trials and a tobacco plantibody against a poultry virus (Newcastle disease) has been approved by the United States Department of Agriculture (USDA) (Vermij & Waltz, 2006).

Anti-tumor antibodies against Burkitt`s lymphoma was expressed in rice and wheat (Ghasempour et al., 2014). Antibodies engineered to bind to Bacillus anthracis was extracted from transgenic strains of tobacco and tested in mice in an experiment. The result of this study showed that the antibodies were effective in fighting B. anthracis strain well for the future in any anthrax epidemic will be a cheap and effective prevention against the disease (Hull et a.l, 2005).

Treatment or cure for rabies through plantibodies has been investigated. A plantibody-based rabies vaccine produced in tobacco was experimentally administered in hamsters to identify whether it could effectively target rabies. According to the plantibody proved to be a safe and economically feasible alternative to the current methods of antibody production in animal systems (Ko et al., 2003).

Another study, tobacco-derived plantibodies were experimentally administered in mice against the Lewis Y antigen found on tumor cells in mice and also in lung, breast, ovarian and colorectal cancer. According to the plantibodies showed a definite positive effect on the cancer-stricken mice by preventing tumor formation in them (Brodzick et al., 2006).

Antibodies against ovarian, testicular and colon cancer as well as melanoma, B-cell lymphoma, and human papillomavirus have already been expressed in transgenic tobacco. These plantibodies are currently being researched and are on their way to being approved for human use. Plantibodies called DoxoRx and RhinoRx for post-cancer therapy and rhinoviruses respectively are in various stages of completion (Fisher et al., 2003).

4.2. Immunization

Active immunization is the resistance developed in an individual as a result of an antigenic stimulus which is otherwise known as adaptive immunity. Passive immunity is the resistance transmitted to recipient in readymade form, preformed antibodies are administered. There is no antigenic stimulus and the recipient's immune system has no active role. The immunity is transient usually lasting only for days or weeks only till the passively transmitted antibodies are metabolized and eliminated. The main advantage of passive immunization is it acts immediately and can be employed in conditions requiring instant immunity (Stroger et al., 2002; Raja et al., 2014).

The production of proteins in plants is a major task in producing pharmaceutical polypeptides. Potential proteins produced include cytokines, hormones, enzymes, epidermal growth factors, interferons, human protein C, and pharmaceutical foodstuff which are considered for oral immunization. Transgenic plants that express antigens in their edible tissue might be used as an inexpensive oral vaccine production and delivery system. Thus, immunization might be possible through the consumption of an "edible vaccine" to provide passive immunization and disease prevention (Mason & Arntzen, 1995).

Genetically engineered plants and plant viruses are also used to produce vaccines against several human diseases for life-threatening infections such as diphtheria, cholera and Acquired immune deficiency syndrome (AIDS) (Moffat, 1995). Some of the proteins are potent inducers of immune responses but some immunizing proteins may not work well when taken orally. Oral vaccines must be protected during passage through the hostile environment of the stomach and intestine to the sites of immune stimulation (Fisher et al., 2003).

4.3. Immunomodulation

Immunomodulation is a molecular technique that allows the interference with cellular metabolism or pathogen infectivity by the ectopic expression of genes encoding antibodies or antibody fragments (De Jaeger et al., 2000). Applications that are relying on modulating antigen levels in vivo are dependent on expression and accumulation in specific subcellular compartments and specific

tissues. Development of crop resistance and passive immunization of plants by expression of pathogen-specific antibodies reduces infection and symptoms caused by viruses and mollicutes, and significant progress has been made towards engineering residence against insects (De Jaeger et al., 2000; Schillberg et al., 2001).

Immunomodulation is a powerful tool for studying or altering the function of an antigen in vivo. Antigen, which may be an enzyme or metabolite, can either be stabilized or blocked in its action. Physiological and morphological changes were observed in plants when an artificial abscisic acid (ABA) sink was created by the production of an ABA-specific scFv in the endoplasmic reticulum of tobacco and potato plants (Conrad & Manteuffel, 2001; Senger et al., 2001).

Antibodies produced in plant-based expression systems are high-value products for pharmaceutical use. Plants represent cost-effective systems for the large-scale production of pharmaceuticals. For complex molecular forms (secretary Immunoglobulin A) sIgA, plants offer a commercially viable system for large-scale production (Ma et al, 1998). Moreover, agro filtration of tobacco was used to produce a diabody against carcinoembryonic antigen (Vaquero et al., 2002).

Transgenic plants are suitable for mAb production because they can be rapidly expanded in commercial products without the high-capital investment associated with traditional mAb bioreactor facilities (Priya et al., 2011). In addition, plantibodies may also prove useful as feed additives or for phytoremediation in human health care (Mason & Arntzen, 1995).

4.4. Bioreactors

Antibodies produced in plants have applications such as the production of vaccine antigens, protein for clinical diagnosis, pharmaceutical and industrial proteins, carbohydrates, vitamins, minerals, biopolymers and food (Sharma & Sharma, 2009). Plant bioreactors are cost-effective and easy for agricultural scale-up. As a result, certain expensive biopharmaceuticals such as human lysosomal enzymes can be produced in plant bioreactors and this is particularly applicable in developing countries. Plant bioreactors have the advantages of having post-translational modifications and lacking of contamination by animal pathogens (Giddings, 2001; Lienard et al., 2007). In recent years, many plant systems have been developed in order to use plants as bioreactors for the production of recombinant antibodies for many purposes (Stoger et al., 2002).

4.5. Treatment of Ebola patients

The production of anti-Ebola virus antibodies has recently been explored in plants (Chen et al., 2011). A high yielding geminivirus-based expression system in the tobacco plant, Nicotiana benthamiana, for the production of a mAb (6D8) that protected animals from Ebola virus infection. Using similar technology and N. benthamiana, (Bhoo et al., 2011) produced an Ebola immune complex (EIC) by fusing Ebola envelope glycoprotein (GP1) to the C-terminus of the heavy chain (HC) of humanized 6D8 mAb that binds specifically to a linear epitope on GP1. Gemini virus vector-mediated co-expression of the GP1-HC fusion and the 6D8 light chain in N. benthamiana leaves produced assembled immunoglobulin, which was purified by protein G affinity chromatography. The resultant recombinant antibody bound the complement factor C1q, indicating immune complex formation. Thereafter, subcutaneous immunization of mice with purified EIC elicited high-level production of anti-Ebola virus antibodies. This was the first published account of an Ebola virus candidate vaccine to be produced in plants (Langreth et al., 2014; Daniel et al., 2016).

Table 1: Pharmaceutical antibodies produced in transgenic plants

Antigen	Plant	Antibody form	Application	Reference
Human chorionic Gonadotrophin	Tobacco	scFv, diabody, chimeric, IgG1	Diagnostic/ contraceptive	Kathuria et al, 2002
Streptococcus surface antigen SAI/II	Tobacco	SigA/G (CaroRx)	Therapeutic (topical)	Ma et al., 2003
Human IgG	Alfalfa	IgG	Diagnostic	Khoudi et al, 1999
Rabies	Tobacco	IgG	Therapeutic	Ko et al., 2003
Herpes simplex virus	Soyabean, Rice	IgG	Therapeutic (topical)	Zeitlin, 1998
Herpes simplex virus	Algae Chlamydomonas chloroplast	One-chain antibody	Therapeutic	Mayfield et al, 2003
Hepatitis B virus	Lettuce	IgG	Vaccine	Kapusta et al, 1999
New castle disease virus	Corn	Surface glycoprotein F	Vaccine	Guerrero- Andrade et al, 2006
Cholera	Tomato	Cholera toxin B subunit (ctb gene)	Oral vaccine	Jiang et al., 2007
Enterovirus	Tomato	Serum IgG VP1	Oral vaccine	Chen et al, 2006
Porcine reproductive and respiratory syndrome virus	Banana	IgG and IgA	Oral immunization	Chan et al, 2013

5. ADVANTAGE, CHALLENGES AND LIMITATION OF PLANTIBODY PRODUCTION

5.1. Advantage and Challenges

Using plants for the production of recombinant proteins has advantages compared with other expression systems such as animal systems, bacterial systems, yeast systems (Ghasempour et al., 2007). Plantibodies work in a similar fashion to mammalian anti-bodies; however, compared to conventional methods using mammalian cells, the use of plants for antibody production offers several unique advantages. Firstly, plants are widespread, abundant, and grow quickly; they usually mature after one season of growth and it is possible to bring the product to the market within a short time. Therefore, the cost of antibodies produced by plants is substantially less than that from their animal counterparts (Sharma et a.l, 2004).

Secondly, plants are less likely to introduce adventitious human or animal pathogens compared to mammalian cells or transgenic animals, thus reducing screening costs for viruses, prions and bacterial toxins (Herbers & Sonnewald, 1999; Lai et al., 2010). Moreover, they do not trigger immune responses in which animal antibodies are prone to do when exposed to foreign/non-self agents and they also produce a relatively high yield of antibodies in a comparatively shorter time (Fisher et al., 2003).

On the other hand, relative ease of genetic manipulation and reduced economic constraints offer added advantage over transgenic animals. Plants might also provide an ideal vehicle for oral delivery of vaccine antigens owing to the presence of thick cell walls composed of cellulose and sugars that may provide protection against degradation by the gastrointestinal tract (Koprowski & Yusibov, 2001; Bindu, 2017).

After lots of benefits, there are some remaining challenges are associated with plantibodies production. During down streaming processes of plantibodies production such as extraction and purification of plantibodies is an important step, covers more than half of the total cost. Thus, the purification system during plantibodies production is very expensive. Currently, the purification system in plant systems, an affinity purification protocol re-quires protein A-based matrix is mainly used (Valdes et al., 2003). So, it is necessary to use alternative economic methods that use oleosin or polymer fusions for the purification of plantibodies (Daniell et al., 2001).

5.2. Limitations of Plantibodies

Despite having so many advantages there are also some limitations to its application. Several studies have shown that people may have negative reactions to plant-derived allergens, fungal contaminations and pesticides used during farming, inability to perform post-translational modification of produced proteins, insufficient expression in some plants, environmental restrictions, allergies or allergic reactions to plants glycoprotein and other plant antigens, mycotoxins produced by impurities, herbicides and plant endogenous metabolites, gene silencing in some cases and different patterns of glycosylation and regulatory issues, particularly for therapeutic proteins requiring approval for human use. Plantibodies are not suitable for infants (Stoger et al., 2002; Doshi et al., 2013; Rani & Usha, 2013; Hashemzade et al., 2014).

CONCLUSION

Transgenic plants have been shown to be the most productive and economical system for making antibodies for human and animal use as they play a key role in providing therapeutics and edible vaccines, which are cheap and easy to administer. Plants have been used for the large-scale production of several recombinant proteins, especially for biopharmaceutical applications with particular emphasis on antibodies and vaccine components. The low-cost, high-scalability and safety characteristics of a plant-based production system offer an attractive alternative for both commercial pharmaceutical products and for manufacturing products. However, purification remains the most significant cost factor for biopharmaceutical production. The technology is not well-practiced in Africa in general and in Ethiopia in particular, especially in the veterinary sector. Even though, there is a great diversity of crops and plants that can be readily explored by the pharmaceutical industry for therapeutic, immune prophylactic, improved livestock productivity and other purposes. In conclusion, the adoption of plants as bioreactors on a larger scale would reduce the cost of antibody therapy and increase the number of patients with access to these treatments thus scholars should advocate the application of plantibodies in the field of veterinary medicine. Application of plantibodies is an important biotechnological breakthrough in the field of medicine therefore it should be encouraged.

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