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Review Article

Arabinogalactan Protein – A Potent Immunostimulator

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ABSTRACT

For the past several years glycoproteins are the subject of interest for the researches because of their abundant presence and diverse functions. Recent researches reported glycoproteins with potential activities such as antiviral, anti-bacterial, anti-tumor, anti-inflammatory, anti-complementary, anti-coagulant, immunostimulatory, anti-ulcer activity etc. Arabinogalactan proteins are group of polysaccharides found almost in all the plants. Many researchers have reported that arabinogalactan protein with potent immune stimulating ability. In recent years arabinogalactan protein is beginning to gain interest as a carrier to deliver drugs. Beside this drug delivery they can also be used to enhance the drug solubility, enhance the drug stability, extend duration of activity etc. This review covers only a small part of the activity of arabinogalactan protein isolated from plants. It mainly focuses on the *invivo* and *invitro* analysis that reveals the immunological activity of arabinogalactan protein.

Key Words: Arabinogalactan, Immunostimulatory, Macrophages, T and B cells

INTRODUCTION

Life threatening infections have become a potential threat in recent years particularly in the immune compromised patients. The enhancement of the host defense mechanism can be recognized as a possible means of reducing these infections. This can be achieved by using immune stimulating polysaccharides isolated from natural sources. In traditional medicine the herbal preparations used posse's significant quantity of polysaccharides or their glycoconjugates. This polysaccharide fraction has various biological activities such as antioxidant, antiviral, antitumor, anticoagulant, antitussive, immunomodulating etc[1]. These polysaccharides stimulate the host immune system mainly by activating various immune cells such as macrophages and T cells. For many years glycoproteins are the subject of interest for the researchers because of their abundant presence and diverse functions. Recent research in the field of immunology has suggested that some of the glycoproteins isolated from natural plant source are found to possess antiviral, anti-bacterial, anti-tumor, anti-inflammatory, anti-complementary, anti-coagulant, immune stimulatory and anti-ulcer activity. Arabinogalactan proteins are the group of hydroxyl proline rich glycoprotein associated with cell wall and the plasma membrane. They play a major role in various functions such as vegetative growth, cellular development, and programmed cell death. However the biological properties of arabinogalactan protein are not yet fully explored[2]. Arabinogalactan proteins are composed of 10% protein and 90% carbohydrates. Arabinogalactan proteins consist of 65-98% carbohydrate covalently linked to the Hydroxyproline, Proline, Serine, Threonine and Alanine rich protein backbone. The polysaccharide fraction of the arabinogalactan protein mainly consists of arabinose and galactose. Arabinogalactan posses various attractive properties such as high solubility in water, biocompatibility, biodegradability, and ease of drug conjugation in an aqueous medium which makes it a potential protein to be explored[3]. This review mainly focus on the overall immuno stimulatory activity of arabinogalactan protein isolated from various plant species.

Coffea Arabica L. (*Coffea Arabica* blend)

Peter et al.,[4] isolated the arabinogalactan protein from coffea Arabica blend using procedure as used by capek et al. Immunostimulatory activity of arabinogalactan protein was compared with instant coffea products. Arabinogalactan protein effectively stimulated pro-TH1 cell immune response and ROS liberation. It was concluded that the arabinogalactan protein mainly contributes to the immunostimulatory activity of instant coffee powder

Young Kanuka Honey (Newzealand Honey)

Swapna et al.,[5] isolated Type II arabinogalactan(>30kda fraction) from young kanuka honey using β-yariv reagent. This arabinogalactan fraction stimulated the release of TNF-α from phorbol 21-myristate 13-acetate (PMA) differentiated THP-1 cells. Thus it was concluded that the arabinogalactan fraction contributed to the immunostimulatory activity of the kanuka honey.

Coffea Arabica L (Rubiaceae)

Nosalova et al.,[1] isolated arabinogalactan protein from *Coffea arabica* using Wolfrom and Anderson procedure. Spleenocytes were isolated 8-12 weeks old female Balb/c mice and cultured in RPM – 1640 medium. The cells were stimulated using the arabinogalactan protein and the release of TNF- α and IL-2 was evaluated using ELISA and ELISPOT assay. It was concluded that arabinogalactan

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protein induced IF-γ and TNF- α in good levels but it was less effective when compared with β D-glucan.

Cereus peruvianus

Leonardo et al.,[6] isolated arabinogalactan protein from fresh stems of *Cereus peruvianus*. Acute gastric lesions were induced in 180-200gm female wistar rats by intra gastric administration of pure ethanol. Omeprezole was used as positive control. Arabinogalactan protein reduced the lesion percentage in a dose depended manner more effectively than omeprezole. Thus it was concluded that arabinogalactan protein can act as a effective anti ulcer remedy.

Soyabean meal (Defatted soybean flour)

Thales et al.,[7] isolated and purified arabinogalactan protein from soyabean meal and tested its gastro protective effect on female wistar rats of weight 180-200gm. Gastric lesions were induced by Et oH. Omeprazole was used as positive control. Omeprazole reduced the lesions by 47% where as arabinogalactan protein reduced lesions by 33, 48 and 71%. From the obtained results it was concluded that arabinogalactan protein act as a potent gastro protective agent.

Artemisia tripartite

Gang Xie et al.,[8] based on the carbohydrate elusion profile selected five polysaccharide fraction and designated as A-I, A-II, A-III, A-IV and A-V. Analysis of these fractions using Yariv reagent revealed that all the fractions except A-I was found to possess Type II arabinogalactan protein. Murine J774. A1 macrophages were tested for NO and ROS production. Fraction A-I and A-V showed highest activity in NO and ROS production at 100-800µg/ ml concentration. To determine the complement fixing activity the plysacharide fraction was compared with heparin a known complement fixing agent. All the fractions inhibited erythrocyte hemolysis activity which indicates the complement fixing activity. When testing Artesemia polysaccharide for neutrophil ROS production on murine bonemarrow neutrophils surprisingly the polysaccharide fractions inhibited the ROS production thus he concluded that these polysaccharide fractions may possess ROS scavenging activity.

Echinacea pallida and *Baptisia tinctoria*

Classen et al.,[9] isolated arabinogalactan protein from water extracts of roots of *Echinacea pallida* and *Baptisia tinctoria* using β- glucosyl yariv reagent. Mouse spleen cells were incubated with various dilution of arabinogalactan protein to test the spleen cell proliferation and IGM production. Arabinogalactan protein exhibited dose dependent increase in spleen cell proliferation and IGM titres. Mouse alveolar macrophages were tested for IL 6 induction and nitrite production. The result revealed dose dependent increase in IL 6 and nitrite production. It was concluded that arabinogalactan protein from *Baptisia tinctoria* showed highest activity when compared to arabinogalactan protein from *Echinacea pallida*.

Larch wood

Mi choi et al.,[10] used arabinogalactan protein purchased from sigma chemicals (St.Louis Mo), Invivo analysis was done in 5-6 weeks old mice and invitro analysis was done using spleen cells from mice, peritoneal macrophages from mice, YAC1 and B16 umor cell lines. Viability study on spleen lymphocytes revealed the significant increase in the viability when incubated with arabinogalactan protein. Cytotoxicity study on spleen lymphocytes and peritoneal macrophages co incubated with YAC-1 and B16 melanoma cells revealed ability of arabinogalactan protein to stimulate NK cytotoxicity. Arabinogalactan protein was also able to increase phagacytic activities of macrophages when tested in zymosan opsonised macrophages. Thus it was concluded that arabinogalactan protein is potent immune stimulator.

Tinospora cordifolia

Gajanan et al.,[11] isolated arabinogalactan protein from the stem of *Tinospora cordifolia*. The mitogenic activity of the arabinogalactan protein was studied using invitro analysis murine spleen cells. The arabinogalactan precipitate obtained from stem of *Tinospora cordifolia* was found to posses' mitogenic activity. This precipitate enhanced the mitogenic activity in B cells but not in the T cells. Thus it was concluded that the aqueous extract of *Tinospora cordifolia* contain B cell activator which may be due to the arabinogalactan protein present in the aqueous extract.

Echinacea purpurea

Luettig et al.,[12] isolated arabinogalactan protein from supernatant cell culture of *Echinacea purpurea*. Male and female C57BL/6 and NMRI nu/nu mice 6-8 weeks old were used for the study. Macrophages isolated from the mice were incubated with 100 µl of arabinogalactan protein in 96 – well flat bottom micro titer plates. After 18-24 hrs the supernatants were tested for TNF-α, IL-1 and IFN β activity. T cells and b cells were isolated from spleen cells and incubated with arabinogalactan protein for 72 hrs to test the proliferation activity. Arabinoglactan protein induced TNF-α, IL-1 and IFN β in a dose dependent manner. It was concluded that AGP from *E.purpurea* significantly induced TNF-α, IL-1 and IFN β production. However it was not significant in increasing the proliferation of T and B cells.

Angelica acutiloba kitagawa

Hiroaki et al.,[13] isolated an anticomplementary arabinogalactan protein (AGIIb-1) from the roots of *Angelica acutiloba kitagawa* with one neutral and two acidic arabinogalactan units. The AGIIb-1 consisted of N-I, N-II, A-I, A-II and 1 Neutral arabinan unit. The AGIIb-I was digested with Exo-α-L-arabino furanosidase. The units NI, NII, AI and AII from AGIIb-I and AF-NI, AF-NII, AF-AI and AF-AII from AF-AGIIb-1 were purified. The samples were mixed with normal human serum. IgM sensidized sheep erythrocytes used to determine residual hemolytic complement (TCH 50) and the total anticomplementary activities was calculated. The Exo-α-L-arabino furanosidase digested AGIIb-I showed potent anticomplementary activity when compared to AGIIb-I

Larix europaea

Beuth *et al.*,[14] used arabinogalactan protein from *Larix europaea* and this study was aimed at determining the inhibition of liver tumor cell colonization. Two animal tumor models, Esb a hidelberg subline of methyl chulanthrene induced DBA12 mouse lymphoma L5178Y

and sarcoma L-1 tumor were used in this study. The mice were preinoculated with arabinogalactan intra peritonally one hour before tumor cells inoculation and regularly administered for 7 days. Lung and liver surface tumor nodules were counted under microscope 14 days after sarcoma inoculation and 7 days after Esb cells inoculation. Arabinogalactan protein administration completely prevented the sarcoma L1 tumor and reduced the dissemination of Esb tumor cells in significant level. However arabinogalactan protein failed to prevent the spreading of tumor cells in other organs such as lungs. Thus it was concluded that the homing of tumor cells in liver can be prevented or decreased using arabinogalactan protein.

CONCLUSION

This review reveals that the arabinogalactan has excellent potential to activate macrophages and also increase the proliferation of T and B cells of the immune system. Hence it can be used as a suitable agent for treating the diseases which affects immune system. This could be a better therapeutic lead for treating certain diseases like rheumatoid arthritis, cancer, tuberculosis, HIV etc. In future this arabinogalactan protein may be considered for improving the bioavailability of the drugs by its carrier bounding nature.

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