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Cultivation of the red algae *Kappaphycus alvarezii* in Brazil and its pharmacological potential

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Abstract: *Kappaphycus alvarezii* (Rhodophyta, Gigartinales) is a red algae widely cultivated as the main source of raw material for the carrageenan industry. This hydrocolloid is normally used in the food industry as a gelling and stabilizing agent. The facility of its commercial farming based on vegetative propagation promoted the success of the aquaculture of this macroalgae that consequently stimulated studies focusing on new potential uses of this resource. This work presents a brief review of the studies related to *K. alvarezii* cultivation in southern and southeastern Brazil, the latest discoveries in the world concerning pharmacological studies with this species and the advantages of the use of carrageenan as a source of dietary fiber, cholesterol reducer, and antioxidant, anti-viral and anti-cancer compounds, as well as the effects in hemagglutination activity.

Introduction

Kappaphycus alvarezii Doty (Doty) ex P.C. Silva is one of the main seaweed cultivated in the world and this species changed the social and economic aspects of several countries in which commercial farms were well established in a relatively short period, such as the Philippines, Indonesia and Tanzania (Hayashi et al., 2010). Commercially known as “cottonii”, is the main raw material for *kappa* carrageenan industry, a hydrocolloid used as a food additive, acting as a gelling, emulsifying, thickening and stabilizing agent in both pharmaceutical and nutraceutical products (Pickering et al., 2007). Among several applications, one of the most important is in the food industry, where the use of carrageenan in dairy products is still growing because of its reactivity with milk proteins. In processed meats, carrageenan can avoid water loss during cooking, acting as a water-binding agent and improving the quality (Bixler & Porse, 2011). According to the FAO database (FAO, 2011), the production of *K. alvarezii* in 2009 was 1,755 tons, worth almost US$ 203 million. Bixler & Porse (2011) mentioned that carrageenan production reached 50,000 tons, profiting US$ 527 million.

Because of the commercial success of *K. alvarezii* for the carrageenan industry and its farming technology based on vegetative propagation, new potential applications are of interest in several branches of the industry (Pickering et al., 2007). Seaweeds are known to be a healthy food with low calorie content and high fiber and mineral content, with significant amounts of protein, vitamins, and trace elements and a wide range of secondary metabolites not found in other organisms. Because of this additional uses as a natural source of functional ingredients, this resource is particularly attractive (Ferraces-Casais et al., 2011; Senthil et al., 2011). In this context, a brief review is presented of the potential uses of *K. alvarezii* and its carrageenan as a dietary fiber, cholesterol reducer, and a source of antioxidant, anti-viral and anti-cancer compounds, as well as its effects on hemagglutination activity.

Cultivation of *Kappaphycus alvarezii*

K. alvarezii has been introduced into tropical regions to supply the commercial demand for raw material for producing carrageenan (Pickering et al., 2007). In Brazil, this species was experimentally introduced on the north coast of São Paulo State in 1995, with the aim of attending this demand, since the natural beds of the native carragenophyte *Hypnea musciformis* (Wulfen) J.V. Lamouroux had been depleted and the country was dependent on imported raw materials. Commercial farming began in 1998 at Ilha Grande Bay and in 2003 at Sepetiba Bay, both located on the south coast of Rio de Janeiro State (Castelar et al., 2009). Subsidized the Brazilian Government, *in vitro* and *in situ* experiments were performed to understand the invasive potential of

K. alvarezii introduced into Brazilian waters and to define the commercial areas as an aid to promoting a responsible introduction. Currently, several new industries have been set up in the area licensed for commercial cultivation (Brazilian Government law IN 185/IBAMA) and a new farming technique using tubular nets has been established in this area (Góes & Reis, 2011).

In 2008, Hayashi et al. (2011) analyzed the feasibility and the environmental risk of cultivating *K. alvarezii* in Santa Catarina state on the southern Brazilian coast. They concluded that the invasive risk is low and that, in the winter, the low water temperature is lethal to the species. The license for cultivation on the southern coast has been analyzed by the Government and, once it is approved, the Federal University of Santa Catarina and the Santa Catarina State Agriculture Enterprise (EPAGRI) intend to establish more than ten farms along the coast using monitoring programs, with the aim of serving as an example of the sustainable development of aquaculture in the state.

Other studies made with this species concern the influence of the farming on the surrounding biota, biofouling processes in sea cultivation, micropropagation cultures, biofilter potential, analysis of cell biology and the influence of environmental factors on the growth and carrageenan production (Pellizzari & Reis, 2011). The interaction with a biostimulant of algal growth has being studied (Loureiro et al., 2011) and investigations to verify cosmetic and pharmacological potential are beginning (unpublished data).

Carrageenan blends as hydrogels for food application

Meena et al. (2009) described the preparation of natural polymers with well-defined properties, such as swelling ability, pH, thermal and degradation ability, which could be utilized in specific food applications, as well as in applications as polymeric carriers or supports. They prepared a hydrogel that exhibited stability in the wide range of pH 1-12 by cross-linking a blend of agar and kappa-carrageenan hydrocolloids with the naturally occurring cross-linker genipin. The ratio of the hydrocolloids and genipin was optimized in the blend as well as in the cross-linked product. Genipin has been used in herbal medicine for its anti-inflammatory, diuretic, choleretic and hemostatic properties and has been approved for food use in Southeastern Asia in Japan, Korea, and Taiwan.

Carrageenan as a dietary fiber and its antiviral and anti-cancer potential

At present, there is a trend to use functional foods that provide health benefits by reducing the risk of chronic diseases, enhancing the ability to manage them and promoting better performance, consequently improving the quality of life. The richness of the algae in minerals, vitamins, bioactive substances, proteins, lipids and polyphenols with antibacterial, antiviral and antifungal properties points to the potential as a supplement in functional foods or as a raw material for the extraction of bioactive compounds (Holdt & Kraan, 2011).

Fayaz et al. (2005) analyzed *K. alvarezii* for its chemical composition and found that this species is rich in protein (16.2% w/w), fiber (29.4% w/w) and carbohydrates (27.4% w/w), with a high proportion of unsaturated fatty acids (44.5% of the total; 11.0% oleic acid, 13.5% *cis*-heptadecenoic acid, 2.3% linoleic acid) and saturated fatty acids (37.0%, composed mainly of heptadecanoic acid). According to them, this species is also a good source of minerals, containing 0.16% calcium, 0.033% iron and 0.016% zinc. The bioavailability of iron, tested via in vitro assays, exhibited higher efficiency under intestinal conditions (pH 7.5) than under stomach conditions (pH 1.35).

In India, where the use of spice is common, *K. alvarezii* powder has been indicated as an ingredient for the preparation of spice to enhance the nutritional quality because of the ash, the protein and crude fiber content, the high amount of Vitamin E and the small amounts of niacin and Vitamin B2 (Senthil et al., 2011).

At the same time, carrageenan is a sulphated polysaccharide that can act as a dietary fiber, clearing the digestive system, protecting the stomach surface membrane, and preventing the effects of potential carcinogens on the intestine. However, carrageenan can inhibit pepsin activity in the stomach and can cause ulcerative colitis in animals (Nisizawa, 2006). Because of this, the Scientific Committee on Food of the European Commission endorsed in 2003 a molecular weight distribution limit for carrageenan for food usage. According to the Commission, the high consumption of low molecular weight carrageenan could provoke peptic ulcer, although nothing has been conclusively proven so far (Hayashi et al., 2010). Indeed, Watson (2008) stated that regulatory authorities had no reason to question the safety of carrageenan although, for suitable consumption, carrageenan should have an average molecular weight of 100,000 Da or higher.

Sulphated polysaccharides have also shown antiviral activity. The major activity is against enveloped viruses, including human pathogens such as HIV (immunodeficiency virus), HSV (herpes simplex virus) and HCMV (cytomegalovirus). The main advantage of this substance is its low toxicity, being appropriate for application as a topical microbicide. One good example of this is the anti-viral agent trade-named Carraguard™, currently undergoing trials in South Africa and Thailand as a microbicidal vaginal gel (Fitton, 2006).

Yuan et al. (2011) have shown that all

chemically-modified *kappa* carrageenan derivatives from *Kappaphycus striatum*, especially the sulfated derivative at a high dose, exhibited enhanced antitumor activity compared to carrageenan oligosaccharides and promoted immunostimulatory activity, including on macrophage phagocytosis, and cellular immunity, especially on spleen lymphocyte proliferation in mices.

Khotimchenko (2010) commented that certain natural sulphated polysaccharides are capable of affecting the early stages of carcinogenesis and neoplastic progression in the period prior to the appearance of an invasive malignant tumor. This substance can be used as a drug carrier for therapy of malignant tumors and as a prophylactic with low toxicity, decreasing the side effects of cytostatic drugs.

Kappaphycus alvarezii **potential as a cholesterol reducer and antioxidant**

The potential of red, green and brown tropical seaweeds, including *K. alvarezii*, as a cholesterol reducer and for cardiovascular protective effects was investigated in rats fed a high-cholesterol/high-fat (HCF) diet supplemented with 5% of seaweed powder. After sixteen weeks, comparison between rats fed the HCF diet alone and rats fed the HCF diet supplemented with *K. alvarezii* powder showed that the latter group had significantly lower body weight gain (-29.1%), plasma total cholesterol (-11.8%), and plasma triacylglyceride (-36.1%), decreased plasma low-density lipoprotein (LDL) cholesterol (-49.3%), increased high-density lipoprotein (HDL) cholesterol (55%) and a decreased atherogenic index (AI), expressed as the ratio of LDL/HDL. The decrease in the AI indicated that the seaweed had a protective effect and could reduce the risk of cardiovascular disease (Mantajun et al., 2010).

The bioactivity of sulphated polysaccharides like carrageenan depends on the degree and position of sulphatation, the molecular weight, and the sugar type or glycosidic branching, among other features. Differences in biological activities can be associated with the modification of the carbohydrates (Yuan et al., 2011). However, the antioxidant properties extend beyond *K. alvarezii* carrageenan; known antioxidant compounds such as polyphenols, β-carotene, and vitamins C and E present in this algae probably help scavenge free radicals, including the hydroxyl radical and superoxide anions (Mantajun et al., 2010). These last-mentioned authors measured the activities of the antioxidant enzymes in the erythrocytes of rats fed with a *K. alvarezii* supplemented diet and found that this type of diet reduced the superoxide dismutase (SOD and glutathione peroxidase (GSH-Px) activities in the erythrocytes to near normal values, suggesting that the seaweed helped to restore the antioxidant enzymes to normal levels.

Crude extracts and the polyphenol content of *Kappaphycus* spp. exhibited reducing power and hydroxyl radical scavenging activity higher than that of standard antioxidants. This antioxidant activity is of particular interest for cosmetic and pharmacological applications (Holdt & Kraan, 2011).

Fayaz et al. (2005) analyzed the antioxidant activity of extracts of *K. alvarezii* and observed that the chloroform:methanol (2:1) extract had 82.5% hydroxyl radical scavenging activity, while the acetone extract had 46.04% scavenging activity, both at a concentration of 1000 ppm. At the same concentration, the acetone extract also showed 63.31% antioxidant activity in the β-carotene linoleic acid system. At the level of 50 ppm, the ethyl acetate extract showed 76% hydroxyl radical scavenging activity, the acetone extract 75.12% and the hexane extract 71.15%.

The antioxidant potential of solvent extracts of *K. alvarezii* was also analyzed by Kumar et al. (2008). They observed that the ethanol extract had a radical-scavenging activity with an IC50 of 3.03 $mg.mL^{-1}$, whereas the water extract had a slightly higher activity, with an IC50 of 4.76 $mg.mL^{-1}$ when analyzed by DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging assay. Good ferrous ion chelating activity was observed for the methanol extract (IC50 3.08 $mg.mL^{-1}$) at 5.0 $mg.mL^{-1}$; this extract showed 67% chelation. The reducing power followed the order: synthetic antioxidant butylated hydroxytoluene (BHT-used as positive control)>methanol>ethanol>ethyl acetate>water>hexane extracts, although the ethanol extract proved to be superior to BHT in the linoleic acid system.

Kappaphycus alvarezii **and carrageenan effects on hemagglutination activity**

Carrageenan with large contents of sulphate shows higher activity as an anticoagulant and blood clearing agent when compared to heparin (Nisizawa, 2006). This is similar to the results of Hung et al. (2009a), who screened Vietnamese marine alga and found strong hemagglutination activity in extracts of the following four red algae: *Gracilaria eucheumatoides, Gracilaria salicornia, Kappaphycus alvarezii* and *Kappaphycus striatum*. According to these authors, the *K. alvarezii* and *K. striatum* extracts strongly agglutinated trypsin- or papain-treated rabbit and sheep erythrocytes, but showed no hemagglutination with human and chicken erythrocytes, independent of treatment with enzymes. These results were further validated in other experiments, where Hung et al. (2009b) evaluated the lectin content in three color morphotypes (brown, red and green) of *K. alvarezii* cultivated in Camranh Bay, Vietnan. They found that, during the northeast monsoon (from September to March), high lectin contents (185-338 $\mu g.g^{-1}$ dry alga) and hemagglutinating activity in rabbit blood (128-1,365 HU.mL^{-1}) were observed in the three morphotypes, coinciding with the period of highest growth rate. Dinh et al. (2009) suggested that macroalgae, including *K. alvarezii*, are a valuable source of lectins with unique carbohydrate-binding specificities that could be used as new probes for carbohydrate structures.

Recommendations

There is no doubt that *K. alvarezii* have a wide range of applications. In the carrageenan industry, this alga is already used as a source of gelling and thickening food additives. However, new pharmacological applications of the bioactive secondary metabolites or applications in the human diet as a functional food with significant amounts of protein, vitamin, mineral, trace elements and dietary fiber that improve health are increasing.

Multidisciplinary research efforts are necessary for improving the knowledge of the products that can be developed from this resource. The improvement of cultivation technologies and environment monitoring, as well as quarantine protocols for translocation and increasing participation of researchers in the formulation of public politics are required. The establishment of a network program should help disseminate the information gathered and facilitate the concerted action of researchers, government, and industry.

Attempts should also be made to improve cultivation technologies for native algae, stimulating their aquaculture, especially in sites where exotic algae can be invasive, such as in the northeastern region of Brazil where there are 3,000 km of reefs in one of the priority areas for worldwide conservation (Castelar et al., 2009). Promising surveys are being carried out with algal species that are cultivated in other countries and, in Brazil, on a small scale, such as *Gracilaria* spp. and *Hypnea musciformis* for carrageenan production and *Ulva* spp. for ulvan production. These resources have a wide range of application as pharmaceuticals and nutraceuticals that, as in the case of exotic algae, could diminish the need for importation by Brazil and serve as a new source of income for littoral communities.

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References

Bixler HJ, Porse H 2011. A decade of change in the seaweed hydrocolloids industry. *J Appl Phycol 23*: 321-335.

Castelar B, Reis RP, Moura A, Kirk R 2009. Invasive potential of off the south coast of Rio de Janeiro state, Brazil: a contribution to environmentally secure cultivation in the tropics. *Bot Mar 52*: 283-289.

Dinh HL, Hori K, Quang NH 2009. Screening and preliminary characterization of hemagglutinins in Vietnamese marine algae. *J Appl Phycol 21*: 89-97.

FAO 2011. Global aquaculture production 1950-2009. http://www.fao.org/fishery/statistics/global-aquaculture-production/query/en, accessed in Oct 2011.

Fayaz M, Namitha KK, Chidambara Murthy KN, Mahadeva Swamy M, Sarada R, Khanam S, Subbarao PV, Ravishankar GA 2005. Chemical composition, iron bioavailability, and antioxidant activity of *Kappaphycus alvarezii* (Doty). *J Agric Food Chem 53*: 792-797.

Ferraces-Casais P, Lage-Yusty MA, Quirós ARB, López-Hernández J 2011. Evaluation of bioactive compounds in fresh edible seaweeds food anal. *Food Anal Method*. DOI: 10.1007/s12161-011-9321-2.

Fitton JH 2006. *Antiviral properties of marine algae.* In: Critchley AT, Ohno M, Largo DB (org.). World seaweed resources-An authoritative reference system. ISBN 90 75000 80 4, UK, ETI Information Services. DVD-Rom.

Góes HG, Reis RP 2011. An initial comparison of tubular netting versus tie-tie methods of cultivation for *Kappaphycus alvarezii* (Rhodophyta, Solieriaceae) on the south coast of Rio de Janeiro State, Brazil. *J Appl Phycol 23*: 607-613.

Hayashi L, Hurtado AQ, Msuya FE, Bleicher-Lhonneur G, Critchley AT 2010. A review of *Kappaphycus alvarezii* farming: prospects and constraints. In: Israel A, Einav R (org.). *Seaweeds and their role in globally changing environments.* Dordrecht Heidelberg London New York: Springer, p. 255-283.

Hayashi L, Santos AA, Faria GSM, Nunes BG, Souza MS, Fonseca ALD, Barreto PLM, Oliveira EC, Bouzon ZL 2011. *Kappaphycus alvarezii* (Rhodophyta, Areschougiaceae) cultivated in subtropical waters in Southern Brazil. *J Appl Phycol 23*: 337-343.

Holdt SL, Kraan S 2011. Bioactive compounds in seaweed: functional food applications and legislation. *J Appl Phycol 23*: 543-597.

Hung LD, Hori K, Nang HQ, Kha T, Hoa LT 2009a. Screening and preliminary characterization of hemagglutinins in Vietnamese marine algae. *J Appl Phycol 21*: 89-97.

Hung LD, Hori K, Nang HQ, Kha T, Hoa LT 2009b. Seasonal changes in growth rate, carrageenan yield and lectin content in the red alga *Kappaphycus alvarezii* cultivated in Camranh Bay, Vietnam. *J Appl Phycol 21*: 265-272.

Khotimchenko YS 2010. The antitumor properties of nonstarch polysaccharides: carrageenans, alginates, and pectins. *Russ J Mar Biol 36*: 401-412.

Kumar SK, Ganesan K, Subba Rao PV 2008. Antioxidant potential of solvent extracts of *Kappaphycus alvarezii* (Doty) Doty-an edible seaweed. *Food Chem 107*: 289-295.

Loureiro RR, Reis RP, Berrogain FD, Critchley AT 2011. Extract powder from the brown alga *Ascophyllum nodosum* (Linnaeus) Le Jolis (AMPEP): a "vaccine-like" effect on *Kappaphycus alvarezii* (Doty) Doty ex P.C. Silva. *J Appl Phycol*. DOI: 10.1007/s10811-011-9735-7.

Matanjun P, Mohamed S, Muhammad K, Mustapha NM 2010. Comparison of cardiovascular protective effects of tropical seaweeds, *Kappaphycus alvarezii, Caulerpa lentillifera,* and *Sargassum polycystum* on high-cholesterol/high-fat diet in rats. *J Med Food 13*: 792-800.

Meena R, Prasad K, Siddhanta AK 2009. Development of a stable hydrogel network based on agar kappa-carrageenan blend cross-linked with genipin. *Food Hydrocolloid 23*: 497-509.

Nisizawa K 2006. Seaweeds kaiso: bountiful harvest from the sea. In: Critchley AT, Ohno M, Largo DB (org.). *World seaweed resources-An authoritive reference system*. ISBN 90 75000 80 4, UK, ETI Information Services. DVD-Rom.

Pellizzari F, Reis RP 2011. Seaweed cultivation on the southern and southeastern Brazilian coast. *Rev Bras Farmacogn 21*: 305-312.

Pickering TD, Skelton P, Sulu JR 2007. Intentional introductions of commercially harvested alien seaweeds. *Bot Mar 50*: 338-350.

Senthil A, Mamatha BS, Vishwanath P, Bhat KK, Ravishankar GA 2011. Studies on development and storage stability of instant spice adjunct mix from seaweed (Eucheuma). *J Food Sci Technol 48*: 712-717.

Watson DB 2008. Public health and carrageenan regulation: a review and analysis. *J Appl Phycol 20*: 505-513.

Yuan H, Song J, Li X, Li N, Liu S 2011. Enhanced immunostimulatory and antitumor activity of diffferent derivatives of *k*-carrageenan oligosaccharides from *Kappaphycus striatum*. *J Appl Phycol 23*: 59-65.

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