

Nutraceuticals in Cancer Therapy

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Benefits promoted by the use of a highly bioavailable fermentation-produced nutraceutical, rich in β -glucans and amino acids, for cancer patients treated with chemotherapy and radiotherapy

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Cancer patients are generally submitted to chemotherapy and radiotherapy, which tend to cause problems related to intense inflammatory processes, malnutrition, nausea and emesis.

Therefore, performing supplementation in these patients is important and necessary, as it favors cancer patients from a nutritional point of view. Studies show that supplementation with **β -glucans** promotes benefits to cancer patients undergoing chemotherapy and radiotherapy.

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Amino acids and β -glucans obtained from fermentation processes proved to be important in the care of cancer patients, because they improve the nutritional parameters and general condition of the patient.

Thus, this work aims to discuss the benefits obtained by cancer patients undergoing chemotherapy and radiotherapy who received supplementation with a fermented nutraceutical rich in **β -glucans and amino acids**.

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In addition, we also discuss the benefits caused by the use of the product called **Bionutri AR1®**, a nutraceutical that contributes to the recovery of nutritional status, indicated for patients with severe malnutrition induced by cancer and the therapeutic approaches chemotherapy and radiotherapy.

We conclude that the use of products capable of promoting supplementation of **β -glucans and amino acids** is extremely beneficial to cancer patients, especially those undergoing chemotherapy and radiotherapy and, therefore, there is an indication supplementation for these patients with the fermented product **Bionutri AR1®**.

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β -glucans

Are polysaccharides that are structural constituents of the yeast cell wall, fungi and some cereals, which are present in fungi, yeasts, algae, bacteria and higher plants, presenting different structures and are differentiated according to the types of chemical bond between the constituent glucose units of the main chain and the branches (Yun *et al.* , 2003; Magnani & Castro-Gómez, 2008).

In recent years, these polymers have been studied with great attention due to their biological actions, mainly with regard to their immunomodulatory effect (Ko & Lin, 2004; Kim *et al.*, 2006).

Yun, C. H., Estrada, A., Van Kessel, A., Park, B. C.,

& Laarveld, B. (2003). Beta-glucan, extracted from oat, enhances disease resistance against bacterial and parasitic infections. *FEMS Immunology and Medical Microbiology*, 35(1), 67-75. [https://doi.org/10.1016/S0928-8244\(02\)00460-1](https://doi.org/10.1016/S0928-8244(02)00460-1)

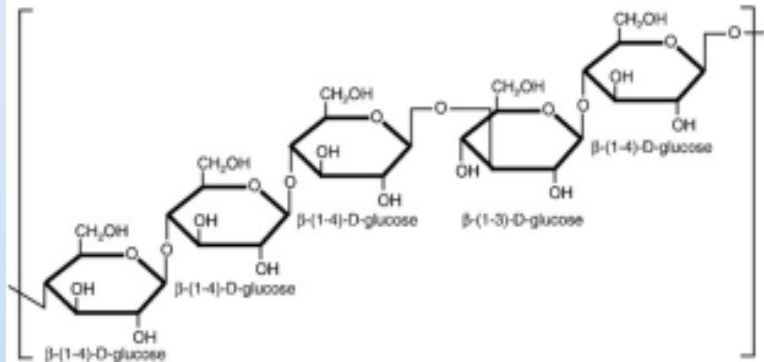
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Magnani, M., & Castro-Gomez, R.J.H. (2008). B

-glucana de *Saccharomyces cerevisiae*: constituição, bioatividade e obtenção. *Semina: Ciências Agrárias, Londrina*, 29(3), 631-650. Ko, Y. T., & Lin, Y. L. (2004). 1,3-beta-glucan quantification by a fluorescence

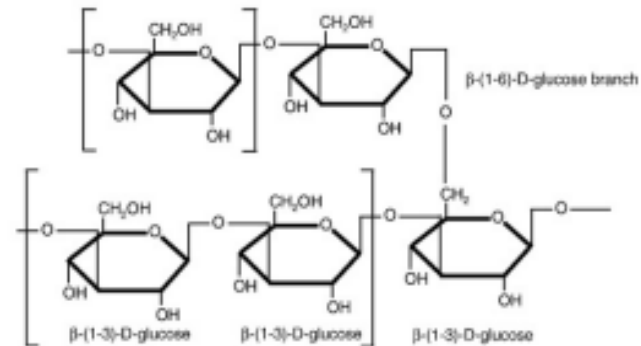
microassay and analysis of its distribution in foods. *Journal of agricultural and food chemistry*, 52(11), 3313-3318. <https://doi.org/10.1021/jf0354085>.

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cereal β -glucan

Polymer of β -(1-4)-D-glycopyranosyl units separated by single β -(1-3)-D-glycopyranosyl units.



yeast β -glucan

Polymer of β -(1-3)-D-glycopyranosyl units with branching at β -(1-6)-D-glycopyranosyl units

β -Glucan type	Structure	Description
Bacterial		Linear β 1,3 glucan (i.e. Curdlan)
Fungal		Short β 1,6 branched, β 1,3 glucan (i.e. Schizophyllan)
Yeast		Long β 1,6 branched, β 1,3-glucan (i.e. WGP β -glucan, Betafectin™)
Cereal		Linear β 1,3/ β 1,4-glucan (i.e oat, barley, rye)

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With regard to the antitumor effect, apparently, **β -glucans** are capable of prevent, delay or reduce the emergence or development of neoplasms (Kuroda & Hara, 1999), a fact that makes.

The association of nutritional therapy with **β -glucans** extracted from the cell wall of microorganisms, fungi and yeasts, which have the ability to promote biomodulation in cancer patients undergoing chemotherapy and radiotherapy (Miadokova *et al.*, 2005).

Kuroda, Y., & Hara, Y. (1999). Antimutagenic and anticarcinogenic activity of tea polyphenols. *Mutation Research*, 436(1), 69–97
[https://doi.org/10.1016/s1383-5742\(98\)00019-2](https://doi.org/10.1016/s1383-5742(98)00019-2)

Miadokova, E., Svidova, S., Vlckova, V., Duhova, V., Prazmariova, E., Tothova, K., Nadova, S., Kogan, G., & Rauko, P. (2005). The role of natura biopolymers in genotoxicity of mutagens/carcinogens elimination. *Biomedical Papers of the Medical Faculty of the University Palacky, Olomouc*, 149, 493–496.

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Di Luzio *et al.* (1979) demonstrated that preparations rich in **β -glucan** produced from fermentation performed by *Saccharomyces cerevisiae* significantly reduced the growth of breast carcinomas and melanomas.

Furthermore, several studies corroborate the findings showing that **β -glucans** promote modulation of the immune functions of the host, even causing the survival of the patient who, in some cases, presents clinical cure, even in patients undergoing chemotherapy and radiotherapy (Moon *et al.*, 2005).

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Kim and Yun (2006) demonstrated that the fermentation process used not only influences but also determines the quality and types of **β -glucan**, relevant factors that should be observed insofar as water-soluble **β -glucans** have been shown to help in the cancer prevention and therapy (Miadokova et al., 2005).

Demir *et al.* (2007) demonstrated that **β -glucans** - produced by *S. cerevisiae* administered for 2 weeks, orally, to 23 women with advanced breast cancer who there was proliferation of monocytes in the peripheral blood, without the occurrence of side effects caused by **β -glucans**.

Miadokova, E., Svidova, S., Vlckova, V., Duhova, V., Prazmariova, E., Tothova, K., Nadova, S., Kogan, G., & Rauko, P. (2005). The role of natural biopolymers in genotoxicity of mutagens/carcinogens elimination. Biomedical Papers of the Medical Faculty of the University Palacky, Olomouc, 149, 493-496.

Demir, G., Klein, H. O., Mandel-Molinas, N., & Tuzuner, N. (2007). Beta glucan induces proliferation and activation of monocytes in peripheral blood of patients with advanced breast cancer. International Immunopharmacology, 7(1), 113–116. <https://doi.org/10.1016/j.intimp.2006.08.011>

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In this sense, Veticka *et al.* (2015) showed that the addition of **β -glucans** in the diet increased serum levels of IgG of cancer patients undergoing treatment, in fact, in cases where supplementation was carried out for three months, the hematopoiesis significantly improved, which caused a significant improvement in the physical and psychological conditions of the patients.

Furthermore, Pohorska *et al.* (2016) showed that supplementation with **β -glucans** considerably increased both the quantity and activity of NK cells, suggesting that continued supplementation with **β -glucans** may help in preventing cancer recurrence.

Pohorska, J., Richter, J., Kral, V., Rajonohova, D. L., Stiborova, I., & Veticka, V. (2016). Reconstruction of NK cells during complex cancer treatment. *Journal of Tumor*, 4, 398–402.

Veticka, V., Richter, J., Kral, V., Dobiasova, L. R., Stiborova I., & Pohorska J. (2015). Regulation of hematopoiesis in cancer patients: placebo-driven, double-blind clinical trials of β -glucan. *Journal of Tumor*. 3: 305–308.

Veticka, V., Vannucci, L., Sima, P., & Richter, J. (2019). Beta Glucan: Supplement or Drug? From Laboratory to Clinical Trials. *Molecules (Basel, Switzerland)*, 24(7), 1251. <https://doi.org/10.3390/molecules24071251>.

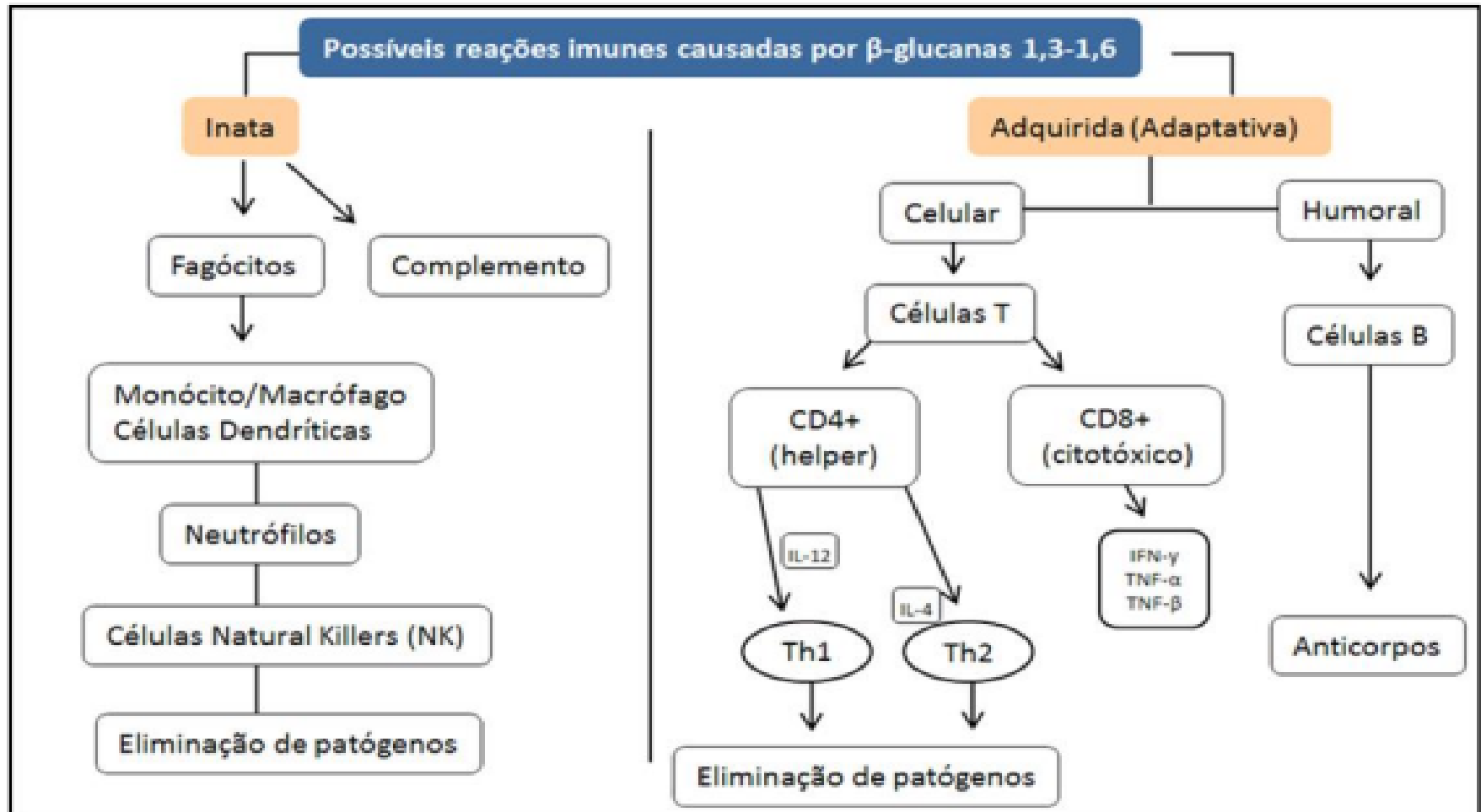
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Fuller *et al.* (2017) showed in a study that had the participation of 49 women, aged between 50 and 70 years, that supplementation with yeast **β -glucans** (Wellmune®) was able to significantly reduce the duration of signs and symptoms caused by respiratory tract infections, an effect that was partly attributed to increased production of interferon- γ .

In addition, Souza *et al* (2018) showed that the administration of the immunomodulatory diet promoted attenuation of the inflammatory process associated with cancer, as well as promoting physical and mental benefits to patients studied oncology.

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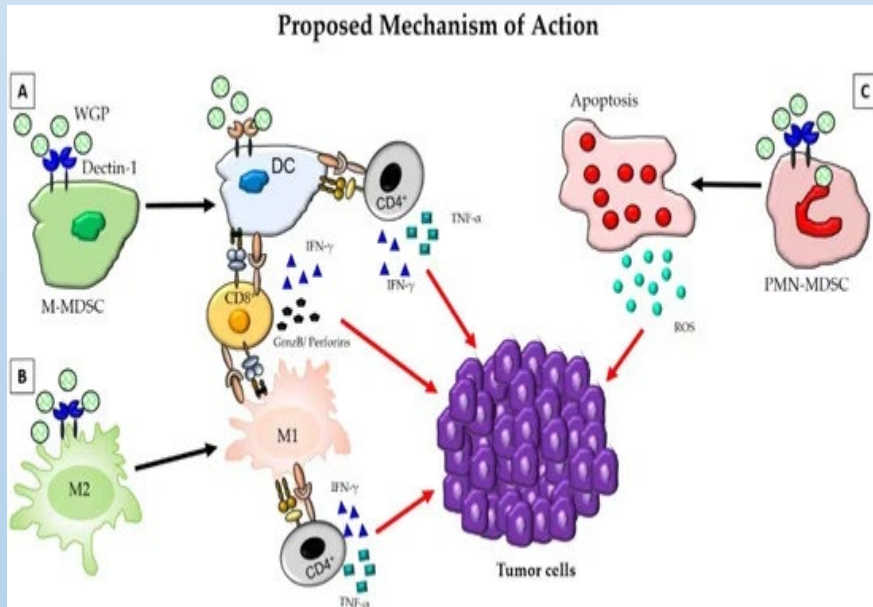
Figura 1 - Reações causadas pelas β -glucanas 1,3-1,6 (Veticka et al., 2019).



Fonte: Autores.

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Published data show that **β -glucans** promote immunostimulatory action in immunocompromised patients and, therefore, cause several beneficial effects to cancer patients, among which we highlight the anti-inflammatory effects. Inflammatory, hypoglycemic, antimutagenic, hypolipidemic, antimicrobial and antitumor (Kogan, 2002; Lin *et al.*, 2004; Kim *et al.*, 2006; Behall *et al.*, 2006).



- Kogan, G., Sandula, J., Korolenko, T. A., Falameeva, O. V., Poteryaeva, O. N., Zhanaeva, S. Y., Levina, O. A., Filatova, T. G., & Kaledin, V. I. (2002). Increased efficiency of Lewis lung carcinoma chemotherapy with a macrophage stimulator—yeast carboxymethyl glucan. *International Immunopharmacology*, 2(6), 775–781. [https://doi.org/10.1016/s1567-5769\(02\)00015-2](https://doi.org/10.1016/s1567-5769(02)00015-2).
- Kim, K. S., & Yun, H. S. (2006). Production of soluble β -glucan from the cell wall of *Saccharomyces cerevisiae*. *Enzyme and Microbial Technology*, New York, 39(3), 496-500.
- Kim, S. Y., Song, H. J., Lee, Y. Y., Cho, K. H., & Roh, Y. K. (2006). Biomedical issues of dietary fiber beta-glucan. *Journal of Korean Medical Science*, 21(5), 781–789. <https://doi.org/10.3346/jkms.2006.21.5.781>.
- Behall, K. M., Scholfield, D. J., Hallfrisch, J., & Sirtori, C. R. (2006). Effect of a highly bioavailable fermentation-produced β -glucan on postprandial plasma glucose and insulin in women. *Diabetes Care*, 29(5), 976–981. <https://doi.org/10.2337/diacare.295976>.

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β -glucans act in several ways to modulate the functioning of the immune system (Figure 1), from Briefly, **β -glucans** are recognized by several receptors present in the membranes of different cells, such as for example, in the membrane of monocytes, macrophages, dendritic cells and Natural Killer cells (NK cells).

Among the most relevant receptors, those of dectin-1, Toll-2 and those of the scavenger receptor family stand out (VETICKA et al., 2019).

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After the binding of **β -glucans** to their receptors, several processes are activated, for example, the effects called pleiotropic, which trigger the production of cytokines and the activation of antibody-mediated responses. In this sense, numerous studies demonstrate that **β -glucans** are able to stimulate B cells, which after being activated promote the secretion of pro-inflammatory cytokines, such as interleukin-8, a process that occurs with participation of dactin-1 receptors, mitogen-activated protein kinase (AMPK) and NF- κ B, in addition to the existence of evidence of the existence of mechanisms involving the regulation of ERK1/2 and the transcription of interleukin-10 (IL-10) (Veticka *et al.*,2019). **β -glucans** promote immunomodulatory effects, which depend on their origin and structure, which is why **β -glucans** can be used in the treatment of patients diagnosed with various diseases related to deficiency of the immune system such as, for example, cancers.

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Supplementation Amino Acid

Glutamine is considered a conditionally essential amino acid in situations of hypercatabolism associated with major surgeries, extensive burns, sepsis and inflammation, where there is negative nitrogen balance and increased rates of proteolysis, and also in immunodeficiency states, frequently found in patients with neoplasms (Oliveira, 2007; Waitzberg, 2008), therefore, the use of **glutamine** in the nutritional supplementation of cancer patients has shown to be a viable option, mainly for the prophylaxis of severe forms of oral mucositis in patients undergoing chemotherapy and/or radiotherapy, allowing the ingestion of food and maintenance of an adequate nutritional status of the patients (Miranda & Souza, 2015).

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Glutamine supplementation reduced the incidence and severity of peripheral neuropathies in patients treated with chemotherapy, with several advantages caused by supplementation being observed, such as, for example, a decrease in the time of hospitalization, mitigation of adverse effects caused by chemotherapy, improvement in nutritional status and recovery lymphocytes and increased patient survival

(Xue **et al.**,2009).

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Boligon and Huth (2010) evaluated the benefits promoted by

glutamine supplementation

in 16 patients (13 from male and 3 female) who were divided into control and test groups, and the control group was composed by patients with a clinical diagnosis of head and neck cancer, undergoing oncological treatment, without any type of nutritional supplementation, while the test group consisted of patients who received supplementation. The patients of the control group presented degrees I to IV, while the patients who received **glutamine** presented only the grades I and II mucositis. In addition, patients in the control group had a reduced Nutritional Risk Index, which did not was observed in patients receiving glutamine supplementation.

Leucine is another amino acid that has been used in the supplementation of cancer patients with the aim of minimize the loss of muscle mass, an event commonly observed in cancer patients (Dillon,2007).

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Bionutri AR1®

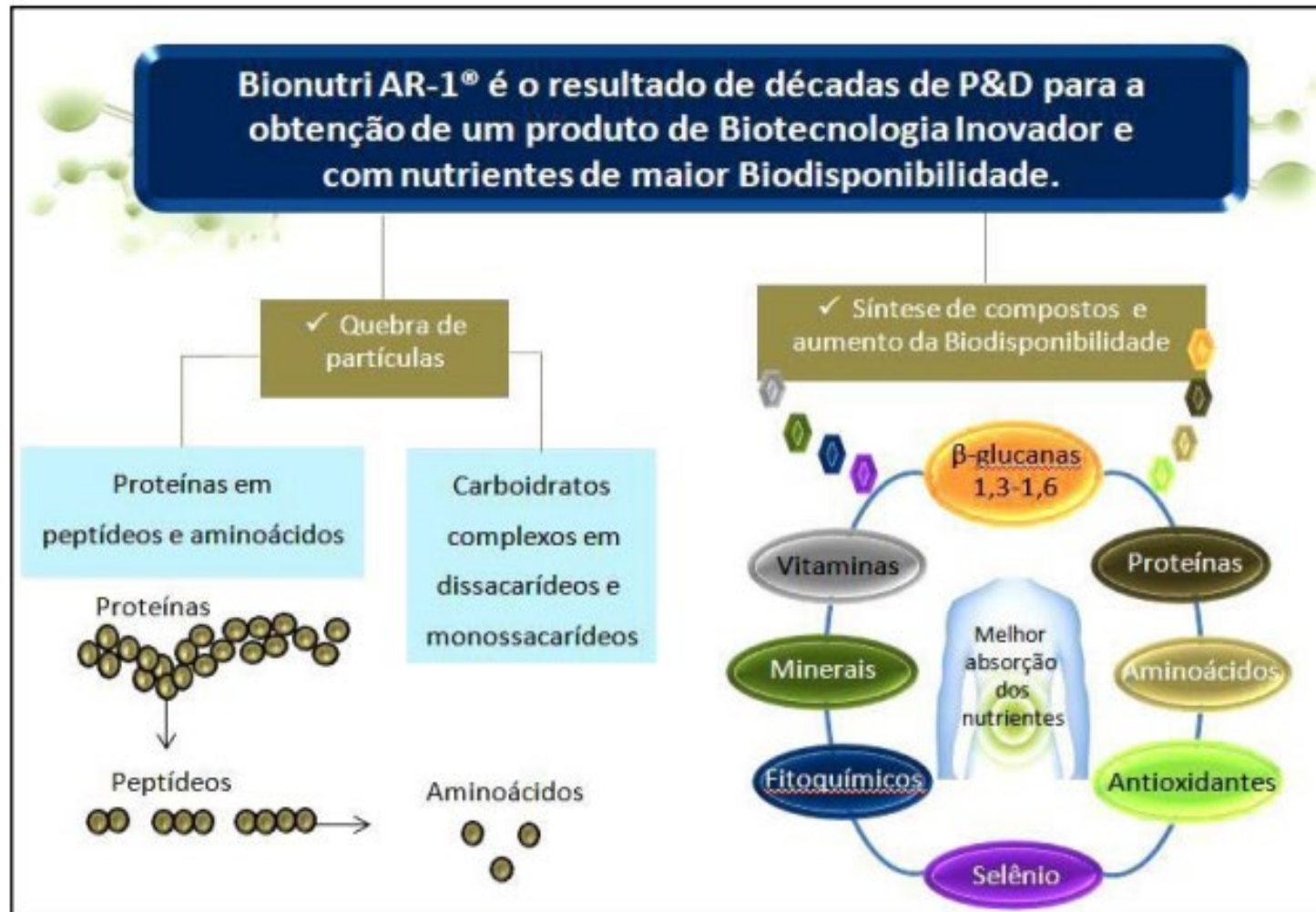
Bionutri AR1®, a nutraceutical manufactured by Pharnutri, has demonstrated the ability to promote an improvement important factor in the nutritional status of cancer patients, a fact that significantly contributes to the reduction of damage caused by chemotherapies and radiotherapies, mainly in the loss of body mass induced by treatments and disease, cancer.

Bionutri AR1® consists of a nutraceutical in powder form, obtained by an exclusive fermentation process that is carried out without the addition of any additive, obtained from an exclusive biotechnology process, nutritionally balanced, for oral and enteral use, valid for 24 months.

In Figure 2, features are illustrated aspects of **Bionutri AR1®** such as, for example, active substances, probable biological actions and high bioavailability components, a fact that increases and guarantees benefits to cancer patients.

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Figura 2 - Mecanismos de ação do Bionutri AR1®.



Fonte: Autores.

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Bionutri AR1® has a digestibility of around 96%, being indicated for the recovery of nutritional status.

It has an immunostimulating and immunomodulatory action, being indicated for patients with cancer-induced malnutrition or with risk for these conditions.

The unique fermentation process used in the elaboration of this product means that the nutrients contained in it are highly bioavailable, a fact that provides better and more complete absorption and assimilation of the nutrients present in the nutraceutical and, consequently, contributes in an important and beneficial way to the recovery of cancer patients, especially those being treated with chemotherapy and radiotherapy.

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Conclusion

Given the above, it is concluded that both supplementation with **β -glucans and fermented amino acids** has demonstrated effective results and in this sense **Bionutri AR1®** presents itself as an alternative supplementation in cancer patients undergoing treatment with chemotherapy and radiotherapy.

The fact that **Bionutri AR1®** is composed of **β -glucans** and several **amino acids** allows cancer patients in chemotherapy and radiotherapy treatment have an adequate nutritional supplementation, in a way that minimizes the state inflammation to which these patients are susceptible.

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I would like to say a big thank you to my team:

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AND I WOULD LIKE TO SAY THAT I FEEL COMPLETELY HONORED TO BE PARTICIPATING IN THIS IMPORTANT EVENT AND BEING ABLE TO PRESENT TO THE INTERNATIONAL SCIENTIFIC COMMUNITY OF NUTRITION AND NUTRACEUTICS OUR PRODUCT BIONUTRIAR1.

THIS PRODUCT IS INTENDED TO REVOLUTIONIZE CANCER TREATMENT IN BRAZIL AND THE WORLD.

THIS IS WHAT WE HAVE EXPERIENCED IN OUR INSTITUTIONS.

THANK YOU VERY MUCH, I WISH EVERYONE A HAPPY CONGRESS AND WE MAKE OURSELVES AT THE DISPOSAL OF THIS HONORED SCIENTIFIC COMMUNITY.

THANK YOU VERY MUCH FOR LISTENING TO ME.

I WISH PEACE TO ALL. HAPPY 2023

BEST REGARDS,

HEZIO JADIR FERNANDES JÚNIOR SÃO PAULO BRAZIL