Revista ARACÊ
ISSN: 2358-2472

MUCOPROTECTIVE ACTIONS OF ANADENANTHERA COLUBRINA GUM IN EXPERIMENTAL INTESTINAL MUCOSITIS

AÇÕES MUCOPROTETORAS DA GOMA DE ANADENANTHERA COLUBRINA NA MUCOSITE INTESTINAL EXPERIMENTAL

ACCIONES MUCOPROTECTORAS DE LA GOMA DE ANADENANTHERA COLUBRINA EN LA MUCOSITIS INTESTINAL EXPERIMENTAL

https://doi.org/10.56238/arev7n11-394

Submission date: 10/30/2025 **Publication Date:** 11/30/2025

Kezia de Souza Nunes, Laisa Divina Vieira Lavor, Fábio Muniz de Rezende, Daniel Correa de Vasconcelos, Michele Maia Assad, Vanessa Moraes da Silva, Kimberlly Menslin Pimenta, Yuri de Oliveira Frota de Siqueira, Rebeca Carolina Lira de Carvalho Otéro, Cintia da Silva Nascimento, Lorena Teles Paiva, Helder Bindá Pimenta

ABSTRACT

Intestinal mucositis is one of the main adverse effects associated with chemotherapy using the antineoplastic agent 5-fluorouracil (5-FU), for which there are still no specific therapies available, with management being predominantly palliative. In this context, natural products have shown promising alternatives in mitigating the side effects resulting from oncological treatment. The gum of Anadenanthera colubrina (Vell.)popularly known as "white angico" is one of these natural compounds, standing out for its previously described antimicrobial, anti-inflammatory, and antioxidant properties. This study aimed to evaluate the potential protective effect of white angico gum, a heteropolysaccharide obtained from the exudate of this legume, in an experimental model of 5-FU-induced intestinal mucositis.

Keywords: Chemotherapy. Inflammation. Fabaceae. Intestinal Mucosa.

RESUMO

A mucosite intestinal é um dos principais efeitos adversos associados à quimioterapia com o agente antineoplásico 5-fluorouracil (5-FU), para o qual ainda não existem terapias específicas disponíveis, sendo o manejo predominantemente paliativo. Nesse contexto, produtos naturais têm demonstrado alternativas promissoras na mitigação dos efeitos colaterais resultantes do tratamento oncológico. A goma de Anadenanthera colubrina (Vell.), popularmente conhecida como “angico-branco”, é um desses compostos naturais, destacando-se por suas propriedades antimicrobianas, anti-inflamatórias e antioxidantes previamente descritas. Este estudo teve como objetivo avaliar o potencial efeito protetor da goma de angico-branco, um heteropolissacarídeo obtido do exsudato dessa leguminosa, em um modelo experimental de mucosite intestinal induzida por 5-FU.

Palavras-chave: Quimioterapia. Inflamação. Fabaceae. Mucosa Intestinal.

RESUMEN

La mucositis intestinal es uno de los principales efectos adversos asociados a la quimioterapia con el agente antineoplásico 5-fluorouracilo (5-FU), para el cual aún no existen

Revista ARACÊ
ISSN: 2358-2472

terapias específicas disponibles, siendo su manejo predominantemente paliativo. En este contexto, los productos naturales han mostrado alternativas prometedoras para mitigar los efectos secundarios derivados del tratamiento oncológico. La goma de Anadenanthera colubrina (Vell.), conocida popularmente como “angico blanco”, es uno de estos compuestos naturales y se destaca por sus propiedades antimicrobianas, antiinflamatorias y antioxidantes previamente descritas. Este estudio tuvo como objetivo evaluar el potencial efecto protector de la goma de angico blanco, un heteropolisacárido obtenido del exudado de esta leguminosa, en un modelo experimental de mucositis intestinal inducida por 5-FU.

Palabras clave: Quimioterapia. Inflamación. Fabaceae. Mucosa Intestinal.

Revista ARACÊ
ISSN: 2358-2472

1 INTRODUCTION

Cancer treatment involves multiple therapeutic modalities, with chemotherapy and radiotherapy being the most widely employed in clinical practice. However, chemotherapy can directly damage the tissues of the oral and gastrointestinal mucosa and induce systemic toxic effects that lead to indirect lesions. These complications, which may be acute or chronic, can occur during or after cancer therapy (WONG, 2014).

Among chemotherapeutic agents, 5-fluorouracil (5-FU) stands out as one of the most commonly used drugs in antineoplastic protocols. Despite its therapeutic efficacy, 5-FU is frequently associated with severe adverse effects on several organ systems, particularly the gastrointestinal tract. It is estimated that 50–80% of patients treated with this drug experience symptoms such as nausea, vomiting, anorexia, and mucositis, which represent the most prevalent complications. Thus, while 5-FU effectively targets malignant cells, it also causes collateral injury to normal tissues (KOIZUMI et al., 2017).

Mucositis is recognized as one of the most significant side effects of chemotherapy. It represents a major clinical challenge that often necessitates dose reduction or temporary discontinuation of cancer therapy, thereby compromising patient survival and increasing hospitalization time and costs (YEUNG et al., 2015).

Histologically, intestinal mucositis is characterized by ulceration, villus atrophy, epithelial apoptosis, and decreased crypt cell proliferation. These alterations manifest clinically as abdominal pain, diarrhea, nausea, and loss of appetite. Given these detrimental effects, there is an urgent need for novel therapeutic or preventive strategies capable of mitigating the severity of mucositis, not only by alleviating symptoms but also by targeting the underlying pathogenic mechanisms (WHITTAKER et al., 2017).

Despite recent progress, antineoplastic therapy still faces major limitations in its effectiveness and continuity, largely due to an incomplete understanding of the complex pathophysiological mechanisms that drive mucositis and other adverse effects (KAWASHIMA et al., 2015).

Considering these implications, the search for natural substances capable of preventing or reducing chemotherapy-induced toxicity has gained attention. Natural products are promising therapeutic alternatives because of their potential to enhance chemotherapy efficacy, minimize side effects, and support systemic detoxification through bioactive compounds with diverse pharmacological properties (SAK, 2014).

Revista ARACÊ
ISSN: 2358-2472

Medicinal plants, in particular, play a pivotal role in traditional medicine due to their rich phytochemical composition, low cost, and accessibility, especially among low-income populations (ARAÚJO et al., 2015). Among these, Anadenanthera colubrina (Vell.), commonly known as “angico branco” and belonging to the Fabaceae family, has drawn scientific interest. The gum obtained from this plant consists of a heteropolysaccharide composed of arabinose (67%), galactose (24%), rhamnose (2%), and glucuronic acid (7%), as well as secondary bioactive metabolites such as phenolic compounds and tannins (PEDONE-BONFIM et al., 2013). Previous studies have shown that A. colubrina possesses anti-inflammatory and wound-healing properties, suggesting that it may provide bioactive molecules of pharmacological relevance for the treatment of inflammatory processes (LIMA et al., 2014; SANTOS et al., 2013).

In this context, the gum of Anadenanthera colubrina emerges as a promising natural compound for managing mucositis. Investigating its biological activity is particularly relevant given the scarcity of experimental studies addressing its therapeutic potential. Moreover, the lack of effective treatments for mucositis underscores the importance of exploring natural products that may enhance therapeutic efficacy and improve the quality of life of patients undergoing chemotherapy.

2 RESULTS

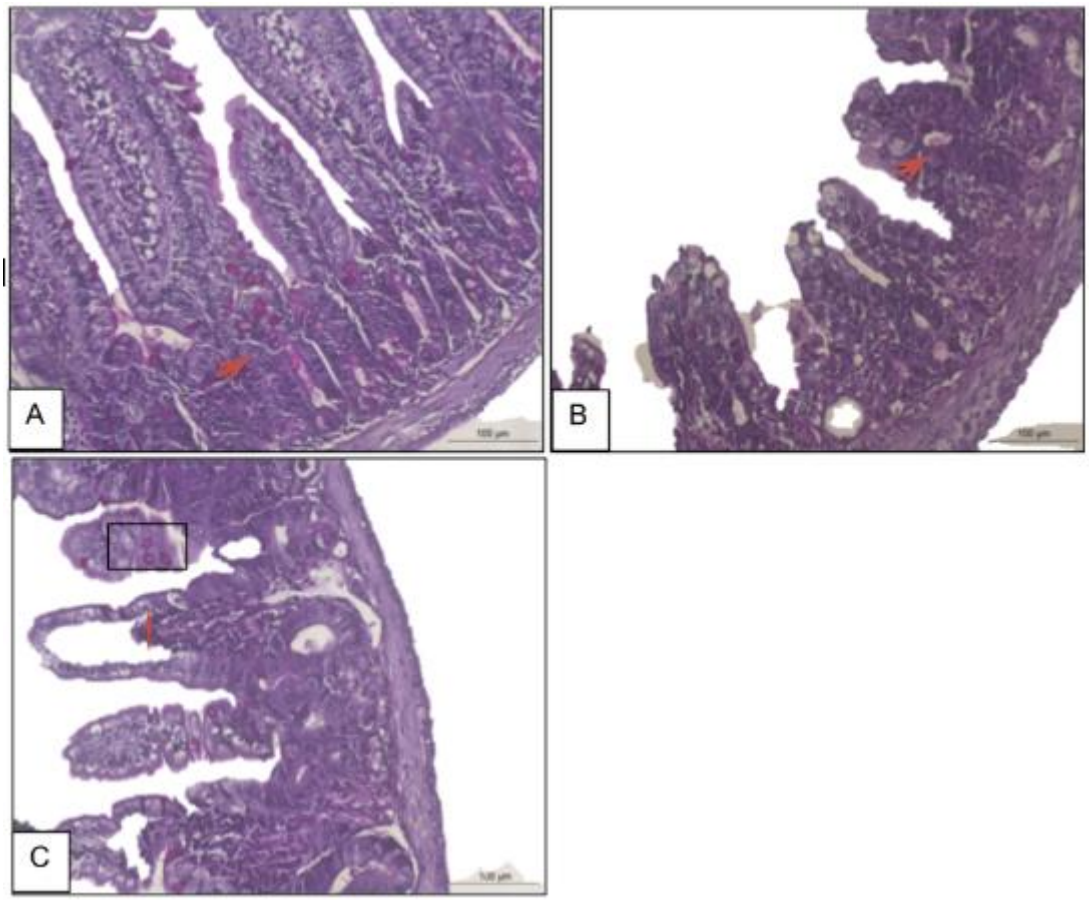
In this experimental study, male Swiss mice (Mus musculus), weighing between 25g and 30g, obtained from the animal facility of the Department of Surgery at the Federal University of Ceará (UFC), were used. Intestinal mucositis was induced in the mice by administering 5-FU, according to the methodology described by Carneiro-Filho et al. (2004), adapted. The experimental protocol was approved by the Ethics Committee on Animal Use (CEUA) of the UFC, under protocol number 3463140518.

The measurement of intestinal mucus production using PAS staining was based on the manufacturer's recommendations (EasyPath). The cells were quantified by counting the number of goblet cells stained in purple-magenta in 10 villi and crypts (SANO et al., 2017).The group treated with white angico gum at a dose of 400 mg/kg showed an increase in the number of magenta-stained goblet cells when compared to the 5-FU group. Similarly, a high presence of these cells was also observed in the saline group.

Revista ARACÊ
ISSN: 2358-2472

Figure 1

Photomicrographs using the PAS method. White angico gum reverses the reduction in mucus production caused by 5-FU in the intestinal mucositis model



Photomicrographs of jejunum sections from mice stained with PAS for visualization of goblet cells. A: Saline; B: 5-FU 450 mg/kg; C: White angico gum 400 mg/kg. 5-FU reduces mucus production, shown by few goblet cells (red arrow), while white angico gum reverses this effect by increasing the number of cells (image C). The panels were obtained at 20x magnification (100µm).

3 DISCUSSION

In the present study, a significant improvement in the histological integrity of the jejunum was observed in animals treated with Anadenanthera colubrina gum (white angico) at a dose of 400 mg/kg. This improvement was evidenced by the partial preservation of goblet cells, responsible for the production of intestinal mucus. In contrast, animals treated exclusively with the chemotherapeutic agent 5-fluorouracil (5-FU) showed intense depletion of these cells, reflecting the destruction of the intestinal mucosal barrier. These findings suggest that white angico gum exerts a protective effect on the mucosal layer, contributing to

Revista ARACÊ
ISSN: 2358-2472

the maintenance of mucin secretion and, consequently, to the preservation of mucosal integrity against the cytotoxic action of 5-FU and bacterial degradation in the intestinal lumen.

Similar results were described by Atiq (2018), who reported complete depletion of mucins in animal models subjected to 5-FU-induced mucositis, contrasting with the significant increase in these compounds after treatment with daidzein, a substance with recognized anti-inflammatory and antioxidant action. These findings reinforce the importance of agents with antioxidant and inflammation-modulating potential in restoring the mucosal layer.

The mucus covering the gastrointestinal epithelium is predominantly composed of mucin glycoproteins, synthesized and secreted by goblet cells. These glycoproteins play an essential role in the lubrication and protection of the intestinal epithelium, acting as a physical and chemical barrier between the luminal content and the underlying tissue, as well as preventing the penetration of pathogens (BANSIL, 2006). Thus, the preservation of goblet cells and mucin production is fundamental for intestinal homeostasis and for defense against inflammatory and infectious processes (ZUO et al., 2015).

As expected, the administration of 5-FU resulted in significant weight loss, one of the most common clinical manifestations of chemotherapy. This weight loss is associated with reduced nutrient absorption, anorexia, diarrhea, and structural changes in the intestinal villi. Daily analysis of the animals' body mass confirmed the nutritional impairment induced by 5-FU, corroborating previous findings in intestinal mucositis models (YONEY; ISIKLI, 2014; CHEN et al., 2012; RAMANI et al., 2010). Despite this, treatment with white angico gum did not prevent the weight loss induced by the chemotherapeutic agent, indicating that, although it exerts local protection on the intestinal mucosa, the compound was not able to completely attenuate the systemic toxicity of 5-FU.

Similar results were reported by Silva (2018), who evaluated the effect of β-caryophyllene on mucositis and did not observe prevention of weight loss. This author associates this finding with a reduction in food digestion and absorption, characteristic of severe intestinal inflammatory states, which can compromise nutritional status and increase vulnerability to infections (LIN et al., 2015).

Similarly, Chen et al. (2016) demonstrated a progressive increase in the diarrhea score in animals treated with 5-FU, a fact that directly contributes to the reduction in body mass. Muscle mass loss and cachexia associated with chemotherapy are related to lower treatment tolerance and reduced overall survival (FEARON; ARENDS; BARACOS, 2013; CRUZ et al., 2010). Additional studies, such as those by Freitas-Blanco et al. (2018) and Carvalho et al.

Revista ARACÊ
ISSN: 2358-2472

(2017), confirm that 5-FU reduces food intake and body weight, even in the presence of mucositis-attenuating agents, which is consistent with the results obtained in this work. Although there are still few specific studies on white angico gum, the results obtained suggest that this heteropolysaccharide may act in protecting the intestinal mucosa by preserving mucus production and the integrity of goblet cells. This action is consistent with the bioactive profile of natural compounds rich in polysaccharides, widely recognized for their biocompatibility, biodegradability, and anti-inflammatory potential (KUMAR et al., 2012; LIU et al., 2008; DAOUB et al., 2018).

Thus, the findings of this study reinforce the role of Anadenanthera colubrina gum as a promising agent in protecting the intestinal mucosa against chemotherapy-induced mucositis, particularly highlighting its ability to preserve mucin secretion and, therefore, the integrity of the epithelial barrier, a crucial aspect for maintaining intestinal function and preventing secondary infections.

4 CONCLUSION

The results obtained in this study demonstrate that the gum from Anadenanthera colubrina exhibits a significant protective effect on the intestinal mucosa in an experimental model of 5-fluorouracil-induced mucositis. Although it did not prevent body weight loss, treatment with the gum promoted histological improvement of the jejunum, with partial preservation of goblet cells and maintenance of mucus production essential factors for the integrity and defense of the intestinal barrier. Thus, the angico branco gum emerges as a promising natural compound for the management of chemotherapy-associated intestinal mucositis, contributing to mucosal protection and restoration of intestinal homeostasis. Further studies are needed to elucidate the molecular mechanisms involved and to evaluate their translational potential in clinical contexts.

REFERENCES

Al-Asmari, A., Al-Zahrani, A., Khan, A., Al-Shahrani, H., & Ali Al Amri, M. (2016). Taurine ameliorates 5-flourouracil-induced intestinal mucositis, hepatorenal and reproductive organ damage in Wistar rats: A biochemical and histological study. Human & Experimental Toxicology, 35(1), 10–20.

Al-Asmari, A. K., Khan, A. Q., Al-Qasim, A. M., & Al-Yousef, Y. (2015). Ascorbic acid attenuates antineoplastic drug 5-fluorouracil induced gastrointestinal toxicity in rats by modulating the expression of inflammatory mediators. Toxicology Reports, 2, 908–916.

Revista ARACÊ
ISSN: 2358-2472

Al-Batran, R., Al-Bayaty, F., Al-Obaidi, M. M. J., Abdualkader, A. M., Hadi, H. A., Ali, H. M., & Abdulla, M. A. (2013). In vivo antioxidant and antiulcer activity of Parkia speciosa ethanolic leaf extract against ethanol-induced gastric ulcer in rats. PLoS ONE, 8(5), Article e64362.

Alderton, W. K., Cooper, C. E., & Knowles, R. G. (2001). Nitric oxide synthases: Structure, function and inhibition. Biochemical Journal, 357, 593–615.

Alves, M. O., Magalhães, S. C. M., & Coelho, B. A. (2017). A regionalização da saúde e a assistência aos usuários com câncer de mama. Saúde e Sociedade, 26(1), 141–154.

Anthony, L., Bowen, J., Jardim, A., Hewson, I., & Sonis, S. (2006). New thoughts on the pathobiology of regimen-related mucosal injury. Supportive Care in Cancer, 14, 516–518.

Araújo, E. R. D., Oliveira, D. C., Soares, T. C., Langassner, S. V. Z., Tavares, J. C. M., & Silva, D. G. K. C. (2015). Avaliação do potencial antimicrobiano de extrato hidroalcoólico e aquoso da espécie Anadenanthera colubrina frente à bactérias gram negativa e gram positiva. Macapá, 5, 66–71.

Atiq, A., Shal, B., Naveed, M., Khan, A., Ali, J., Zeeshan, S., Al-Sharari, S. D., Kim, Y. S., & Khan, S. (2019). Diadzein ameliorates 5-fluorouracil-induced intestinal mucositis by suppressing oxidative stress and inflammatory mediators in rodents. European Journal of Pharmacology, 843, 292–306.

Baizabal-Aguirre, V. M., Rosales, C., López-Macías, C., & Gómez, M. I. (2016). Control and resolution mechanisms of the inflammatory response 2016. Mediators of Inflammation, 2016, Article 1375182.

Balmant, B. D., Araújo, E. O. N., Yabuki, D., Novais, A. B., Genaro, S. C., Laposy, C. B., Goiozo, P. F. I., Chacur, M. G. M., Giuffrida, R., & Reis, L. S. L. S. (2018). Effects of L-arginine supplementation on leukogram, inflammatory bowel infiltrates and immunoglobulins with 5-FU use in rats. Nutrition and Cancer, 70(2), 249–256.

Bansil, R., & Turner, B. S. (2006). Mucin structure, aggregation, physiological functions and biomedical applications. Current Opinion in Colloid & Interface Science, 11, 164–170.

Barbosa, K. B., Costa, N. M., Alfenas, R. C., Sérgio Oliveira de Paula, S. O., Minim, V. P., & Bressan, J. (2010). Estresse oxidativo: Conceito, implicações e fatores modulatórios. Revista de Nutrição, 23, 629–643.

Bastos, C. C. C. (2014). Efeitos da formulação mucoadesiva de Bidens pilosa L. (Asteraceae) e Curcuma longa L. (Zingiberaceae) no tratamento da mucosite intestinal [Dissertação de mestrado, Universidade Federal de Goiás].

Bonomi, M., & Batt, K. (2015). Supportive management of mucositis and metabolic derangements in head and neck cancer patients. Cancers, 7, 1743–1757.

Bradley, P. P., Christensen, R. D., Priebat, D. A., & Rothstein, G. (1982). Measurement of cutaneous inflammation: Estimation of neutrophil content with an enzyme marker. Journal of Investigative Dermatology, 78(3), 206–209.

Bryan, N. S., & Grisham, M. B. (2007). Methods to detect nitric oxide and its metabolites in biological samples. Free Radical Biology and Medicine, 43, 645–657.

Revista ARACÊ
ISSN: 2358-2472

Calder, P. C. (2015). Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance. Biochimica et Biophysica Acta, 1851, 469–484.

Candido, J., & Hagemann, T. (2013). Cancer-related inflammation. Journal of Clinical Immunology, 33, 79–84.

Cardoso, C. R., Provinciatto, P. R., Godoi, D. F., Ferreira, B. R., Teixeira, G., Rossi, M. A., Cunha, F. Q., & Silva, J. S. (2009). IL-4 regulates susceptibility to intestinal inflammation in murine food allergy. American Journal of Physiology. Gastrointestinal and Liver Physiology, 296, G593–G600.

Carneiro-Filho, B. A., Lima, I. P., Araujo, D. H., Cavalcante, M. C., Carvalho, G. H., Brito, G. A., Lima, V., Monteiro, S. M., Santos, F. N., Ribeiro, R. A., & Lima, A. A. (2004). Intestinal barrier function and secretion in methotrexate induced rat intestinal mucositis. Digestive Diseases and Sciences, 49(1), 65–72.

Carvalho, M. D., Moura, L., Prado, R. R., Escalante, J. C., Schmidt, M. I., & Duncan, B. B. (2014). Mortalidade por doenças crônicas não transmissíveis no Brasil e suas regiões, 2000 a 2011. Epidemiologia e Serviços de Saúde, 23, 599–608.

Carvalho, R. D., Breyer, N., Menezes-Garcia, Z., Rodrigues, N. M., Lemos, L., Maioli, T. U., da Gloria Souza, D., Carmona, D., de Faria, A. M., Langella, P., Chatel, J. M., Bermúdez-Humarán, L. G., Figueiredo, H. C., Azevedo, V., & de Azevedo, M. S. (2017). Secretion of biologically active pancreatitis-associated protein I (PAP) by genetically modified dairy Lactococcus lactis NZ9000 in the prevention of intestinal mucositis. Microbial Cell Factories, 16, Article 1.

Chaveli-López, B., & Bagán-Sebastián, J. V. (2016). Treatment of oral mucositis due to chemotherapy. Journal of Clinical and Experimental Dentistry, 8, e201–e209.

Chen, H., Yu, M., Li, M., Zhao, R., Zhu, Q., Zhou, W., Lu, M., Lu, Y., Zheng, T., Jiang, J., Zhao, W., Xiang, K., Jia, W., & Liu, L. (2012). Polymorphic variations in manganese superoxide dismutase (MnSOD), glutathione peroxidase-1 (GPX1), and catalase (CAT) contribute to elevated plasma triglyceride levels in Chinese patients with type 2 diabetes or diabetic cardiovascular disease. Molecular and Cellular Biochemistry, 363, 85–91.

Chen, P., Mancini, M., Sonis, S. T., Fernandez-Martinez, J., Liu, J., Cohen, E. E. W., & Toback, F. G. (2016). A novel peptide for simultaneously enhanced treatment of head and neck cancer and mitigation of oral mucositis. PLoS ONE, 11(4), Article e0153308.

Pimenta, H. B., et al. (2019). Evaluation of the effect of angico polysaccharide Anadenanthera colubrina (Vell.) in experimental model of intestinal mucosite induced by 5-fluorouracil in mice. The FASEB Journal, 33(S1), 767.38.