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A literature review on the medicinal properties and toxicological profile of *Costus spicatus* plant

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ABSTRACT

A literature review was undertaken by analyzing distinguished books, undergraduate and postgraduate theses, and peer-reviewed scientific articles and by consulting worldwide accepted scientific databases, such as Medline, PubMed, Lilacs, Embase Scopus, Web of Science, SCIELO, Google Scholar and ISI. Medicinal plants used in the coadjuvant treatment of various diseases. *Costus spicatus* (Jacq.) Sw. (Costaceae) is used by the Amazonian population to treat inflammation, pain and other pathological manifestations such as diabetes. This review clearly indicates the need to perform scientific studies with medicinal flora highlighting potential for *Costus spicatus* plant due to its antioxidant, anti-inflammatory and hypoglycemic properties.

Keywords: *Costus spicatus*, diabetes, hypoglycemic, antioxidant, anti-inflammatory.

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INTRODUCTION

Since time immemorial, man looking in nature resources to improve their living conditions to thus increase their chances of survival by improving their health. In all ages and cultures, he learned to take advantage of local natural resources (Brazil, phytotherapy in SUS, 2006). According to the World Health Organization (WHO, 2007) it is estimated that 80% of the world population, somehow uses plants to treat illnesses. Despite the wide variety of synthetic drugs (many originating related to the natural environment), the interest in knowledge of the morphology, chemical composition and pharmacological properties has increased especially when it comes to Brazilian plants. Brazil is custodian of huge rich flora in raw material that has aroused the interest of researchers from various universities and institutions dedicated to herbal medicine. The Amazon region is considered inexhaustible source of therapeutic potential with the use of medicinal plants (Martins, 2006).The pharmacological potential of medicinal plants may be more economical output for treating various diseases including chronic diseases. In developing countries, about 80% of deaths are caused by chronic diseases (OPS, 2005). Among these Diabetes mellitus, has called attention to its growth in the number of occurrences. The World Health Organization estimates that annually occur 3 million deaths caused by diabetes. There are also consequences as 1 million amputations, 500 000 cases of kidney disease, 300 000 blindness, 285 million people worldwide with diabetes, and by 2030 will be 435 million diabetics most in developing countries. There is an estimate that, they said the disease related problems generate annual spending of $ 150 billion (IDF, 2009).In Brazil there are 10 to 12 million people with diabetes. Of these, type I 10% (100% of diagnosed, treated 100%) and 90% type II. Diabetes and its cardiovascular and renal effects are now the highest impact factors in public health leading to a high social and economic cost. According to the Ministry of Health (MOH), 1/3 of the patients buy products to treat diabetes in pharmacy, while the majority receive government free products, which requires the Brazilian government high spending on treating diabetes and its consequences. The MS expects growth of 60% of deaths in cases of diabetes in Brazil by 2025 (IDF, 2009). The choice of plants with hypoglycemic activity is mainly due to the fact that diabetes is in Brazil one of the diseases with higher mortality rates, high prevalence in adults and have high medical and social costs (IDF, 2009).Diabetes mellitus dysfunction is recognized as a heterogeneous group of disorders with the common elements of hyperglycaemia and glucose intolerance, is caused by deficiency of production and / or action of insulin, which leads to acute symptoms and chronic complications characteristics. This disorder involving the metabolism of glucose, fats and proteins and have serious consequences, both when it appears as when rapidly settles slowly. Nowadays it constitutes a public health problem by the number of people who have the disease. Diabetes mellitus

is classified based on the etiology, clinical presentation of disease in three types; Type I diabetes, Type II diabetes, and gestational diabetes (Guyton, 2011).Diabetes is directly related to the functioning of the pancreas. Single mixed gland of the human body, 98% exocrine (producing pancreatic juice) and 2% endocrine portion are represented by four cell types: type alpha cells, beta cell type, delta type cells and cells type F. (Guyton, 2011).

Type I diabetes, also called insulin-dependent diabetes, immune-mediated or juvenile diabetes, is characterized as an autoimmune disease that irreversibly injured the beta cells. Thus, they are detected in the blood of low levels patients insulin hormone and the first months after the onset of disease, several antibodies, the most important being anti-pancreatic islets antibody, which destroys the enzyme beta cells. (Guyton, 2011) The disease can affect people of any age, but usually occurs in children or young adults. Type I diabetes is an endocrine and metabolic complications most common in childhood. People with this type require injections of insulin daily to control blood glucose levels. Without insulin, people with type I diabetes do not survive. (American Diabetes Association, 2009) Type II diabetes is characterized by insulin resistance and relative insulin deficiency. The diagnosis of Type II diabetes usually occurs after the age of 40 years, but may occur earlier, especially in populations with high prevalence of diabetes. There are reports of increased of children developing Type II diabetes. Type II diabetes can remain undetected or are asymptomatic for many years and diagnosis is often occurs after complications associated by examination of glucose levels in blood or urine. It is often, but not always, associated with obesity, which in turn may cause insulin resistance and lead to elevated levels of blood glucose. (Nascimento et al., 2016a) There are several possible factors for the development of Type II diabetes. It is known that family is strong, but the major susceptibility genes have not been identified. These factors include: Inactivity obesity, poor diet, increasing age, insulin resistance, family history of diabetes. In contrast to Type I diabetes, people with Type II diabetes are not dependent on exogenous insulin and not prone to ketosis but may require insulin for the control of hyperglycemia if this is not achieved by diet alone or with oral anti-diabetics. The increasing prevalence of Type II diabetes is associated with rapid cultural and social changes, aging population, increasing urbanization, dietary changes, reduced physical activity and unhealthy life and other behavioral patterns (IDF, 2009).

Hyperglycemia is increased glucose levels in the blood. The main cause of hyperglycemia is diabetes occurring due to pancreatic dysfunction due to the absence, decreased or inadequate action of insulin, the hormone responsible for the maintenance of glucose levels in blood (less than 110 mg/ dL and fasting to 140 mg / dL when measured blood glucose 2 hours after meals) (Roche, 2003).Increased blood sugar is harmful to the body and it tries, through various compensatory

mechanisms, reduce blood glucose. One of these mechanisms is to send glucose to the kidneys to be excreted in the urine every time exceeds 160-180 mg / dL in the blood. Then comes the first sign of hyperglycemia: polyuria, which is excess urine. The patient removes glucose and plenty of water, with excessive thirst, a classic sign known as polydipsia. (American Diabetes Association, 2009) Despite being high blood glucose occurs while the reduction of glucose in the brain which causes hungry (polyphagia), because the body thinks are not fed. In addition to these symptoms well known, there are others: pain, numbness and tingling in the legs, blurred and blurred vision, itching in the genital region and decreased healing. Among the most important complications of hyperglycemia are: retinopathy (eye problem), nephropathy (renal failure), neuropathy (nerve impairment) and angiopathy (degeneration of blood vessels that occurs in the whole body). (Roche, 2003)

Gut hormones send information about incoming nutrients to the rest of the body and thereby control many aspects of metabolism. The secretion of ghrelin and glucagon-like protein (GLP)-1, two hormones with opposite secretory patterns and opposite actions on multiple targets, is controlled by a limited number of G-protein coupled receptors (GPCRs); half of which recognize and bind dietary nutrient metabolites, metabolites generated by gut microbiota, and metabolites of the host's intermediary metabolism. Most metabolite GPCRs controlling ghrelin secretion are inhibitory, whereas all metabolite receptors controlling GLP-1 secretion are stimulatory. This dichotomy in metabolite sensor function, which is obtained through a combination of differential expression and cell-dependent signaling bias, offers pharmacological targets to stimulate GLP-1 and inhibit ghrelin through the same mechanism. (Engelstoft and Schwartz, 2016) Diabetic retinopathy (DR) is a serious complication of diabetes mellitus affecting about one third of diabetic adults. Despite its prevalence, treatment options are limited and often implemented only in the later stages of the disease. To date, the pathogenesis of DR has been extensively characterized in the context of elevated glucose, insulin, and VEGF signaling, although a growing number of other growth factors and molecules, including transforming growth factor-β (TGF-β) are being recognized as important contributors and/or therapeutic targets. (Wheeler and Lee, 2016)

Tsuneki et al (2016) suggested that modern lifestyles prolong daily activities into the nighttime, disrupting circadian rhythms, which may cause sleep disturbances. Sleep disturbances have been implicated in the dysregulation of blood glucose levels and reported to increase the risk of type 2 diabetes (T2D) and diabetic complications. Sleep disorders are treated using anti-insomnia drugs that target ionotropic and G protein-coupled receptors (GPCRs), including γ-aminobutyric acid (GABA) agonists, melatonin agonists, and orexin receptor antagonists. A deeper understanding of the effects of these medications on glucose metabolism and their underlying mechanisms of action is

crucial for the treatment of diabetic patients with sleep disorders. In Brazil, it is believed that ¼ of the eight billion pharmaceutical industry national income arising in 1996 were derived from medicinal plants. However, little information is available about the potential risk of certain medicinal plants for human health, although many contain chemicals known to be mutagenic and / or carcinogenic. Besides the low cost, they are found in great variety in our country native species that are used empirically for millennia. (Nascimento et al., 2016c)

Some examples of plants popularly used in diabetes treatment are: Rosemary (*Rosmarinus officinalis* roscoe), mulberry (*Morus alba*), beggarticks (*Bidens gardneri*), parsley (*Petroselinum crispum*) Pata-de-vaca (*Bauhinia forficata*), Ironwood (*Caesalpinia ferrea*), Grageru (*Chrisobalanus icaco)*, insulin (*Cissus sicyoides*), Sucupira (*Bowdichia virgilioides*), among others. (Damasceno, 2005) Medicinal plants encompass a rich source of active compounds that can neutralize snake venoms or toxins. *Costus spicatus* (Jacq.) Sw. (Costaceae) is used by the Amazonian population to treat inflammation, pain and other pathological manifestations. The *Costus spicatus* Swartz plant (Family: Zinziberaceae / Costaceae), popularly known in Brazil “cane of the marsh”, is a native species found in humid South of Mexico, Yucatan, Costa Rica, northern Colombia and Brazil. The cane of the swamp name is used to designate two species of *Costus: Costus spiralis* Rosc. and *Costus spicatus* Swartz, since both have the same use in popular therapy. Found throughout the Brazilian territory, *Costus spicatus* is a shrub, perennial, rhizomatous, erect, unbranched, of 1-2m tall, native mainly in the Atlantic Forest and Amazon region. Presents alternating leaves, membranous, Papyraceous provided with sheaths, velvety on both sides, 25-40 cm long and 6-10 cm wide. It has inflorescences in terminal spikes in strobili format, with large showy bracts of red color, which protect the yellowish flowers. Multiply both by seeds and by rhizomes. Its easy cultivation allows use of all parts of this plant. Costus spicatus Swartz (Costaceae), commonly called "cana-do-brejo'" in Brazil's northeast, is a medicinal plant found in wet coastal forests. In folk medicine an infusion of the aerial parts is taken to treat inflammation and pain. (Quintans Júnior, et al., 2010) One of its uses is the ornamental gardens both as to cut flower production, as can be seen in figure 3 its beauty. Its leaves, stems and rhizomes are used in traditional medicine a long time, especially in the Amazon region (Gasparri, 2005). In this region many species are used as spices, seasonings, drugs, flavoring agents and a source of certain dyes (Gasparri, 2005). Many species of the genus Alpinia, Amomum, Curcuma, Costus, Caempferia and Zingiber are present in traditionally prepared tonics and ingredients called 'potions', which are commercially available.

It is popularly used for its purifying and diuretic action, for relief of urinary infections and to expel kidney stones. Also for treating colds, sore throat, dysentery, diarrhea and treatment of

diabetes. Phytochemical analysis of rhizomes *Costus spicatus* revealed the presence of flavonoids, flavo-carbohydrates, saponins and sapogenins. The antimicrobial action, anti-inflammatory and diuretic activities also proven. But his hipogliceminante effect was not studied. (Antoniolli, 2007)
This plant has attracted the attention of researchers because it was found in the rhizomes just a new source of diosgenin, a precursor of steroid hormones. (Antoniolli, 2007) Also, for phytochemical studies of the aerial parts of the plant, have been described recently, two new glycosidic flavonoids: tamarixetin the Kaempferol *3*-O-*neohesperidoside* and*3*-O-*neohesperidoside*. Other compounds known enough as quercetin 3-O-neohesperidoside and six were identified. These glycosidic flavonoids had proven anti-inflammatory activity. However, there are no studies that prove the effectiveness and safety of using this plant for therapeutic purposes. (Gasparri, 2005) In 2008, the Ministry of Health created the National List of Medicinal Interest SUS Plants (Renisus), based on the list of plant species already used in state and municipal health services, traditional and popular knowledge and chemical studies and pharmacological . These species have the potential to advance in the stages of the production chain and generate products of interest to SUS. Technical Anvisa and the Ministry of Health selected by region, medicinal plants with indications of use and according to the categories of the International Classification of Diseases (ICD-10). Exotic or endangered species were excluded from the list.(Badke, 2012) The aim of this study is to conduct a review of the medical and toxicological properties of the plant *Costus spicatus* which is in the National List of Medicinal Plants of Interest to the SUS (Renisus).

MATERIALS AND METHODS

This work was developed from a review of the literature on Medline, PubMed, Lilacs, Embase Scopus, Web of Science, SCIELO, Google Scholar and ISI in the period between 2000 and 2016. The keywords used were "diabetes," "natural products" and "Costus spicatus ". Exclusion criteria: articles published before 2000. After reading the titles of the articles, it was noted that some of them were repeated in the different bases and others did not meet the study criteria. The most relevant articles were selected for reading the summary and excluding those that were not related to the purpose of this study. After reading the abstracts, articles were selected that potentially met the criteria originally proposed and which were read in full (detailed in the references of this scientific article.

RESULTS

The aim of this study was to present and discuss the findings in the literature regarding the medicinal properties of the plant *Costus spicatus* from its use in folk medicine level in addition to consider the toxicological profile of said plant under study. In this context, the articles were read carefully selected and grouped into five categories: a) the ratio of herbal medicines in the treatment of diseases; b)

prevalence and characterization of diabetes as a disease which affects a lot of people around the world; c) the importance of the investigation of the properties of plants with medicinal potential; d) Phytochemical characteristics of *Costus spicatus* plant; e) The use of *Costus spicatus* plant in the treatment of diabetes.

DISCUSSION

The Ethnopharmacology of Brazil is extremely interesting because of the region's high level of cultural and medicinal plant diversity. In literature level is observed even though little work has been done to document the medicinal traditional practices related to the medicinal potential of the Brazilian flora. This review aims to provide an overview of the current knowledge of plants medicinal how, highlighting the *Costus spicatus* which is of investigative interest to the SUS in order to better understand the medicinal use of this plant, identify research gaps, and suggest directions for further research. Species can arise via the divisive effects of allopatry as well as due to ecological and/or reproductive character displacement within sympatric populations. Two separate lineages of Costaceae are native to the Neotropics; an early-diverging clade endemic to South America (consisting of ca. 16 species in the genera Monocostus, Dimerocostus and Chamaecostus); and the Neotropical Costus clade (ca. 50 species), a diverse assemblage of understory herbs comprising nearly half of total familial species richness.

The genus *Costus spicatus* belongs to Costus family. They are perennial tropical plants. They are often distinguished from plants of the genus Zingiber the spiraling growth of their stems. Besides the *Costus spictus* we can mention the *Costus pulverulents* and *Costus speciosus* who already have some properties of pharmacological interest described. *Costus pulverulentus* (Costaceae), a species endemic to Mexico, is used for the empirical treatment of cancer, pain, and inflammation. (Alonso-Castro et. al., 2016) *Costus spicatus* Sw. (Costaceae) is a prominent medicinal herb used by Dominicans in the Dominican Republic and the United States for the treatment of diabetes, a growing epidemic in the Hispanic community. An ethnobotanical survey of the Dominican community in New York City revealed the popular use of a tea from the insulina plant to treat hyperglycemia. Insulina was identified as *Costus spicatus*. *Costus pulverulentus* C. Presl (Costaceae), a species endemic to Mexico, is used for the empirical treatment of cancer, pain, and inflammation. Alonso-Castro et al (2016) related that *C. pulverulents* exerts moderate cytotoxic effects in human cancer cells, moderate anti-inflammatory and antinociceptive effects. *C. pulverulentus* induces antinociceptive effects without inducing sedation. Nascimento et al (2016a) related that the aqueous extract of *Costus spicatus* has a hypoglycemic effect possibly related to the phytochemical compounds of *Costus spicatus* plant leaves include glycosides, tannins, saponins, terpenoids, phenolics, flavonoids,

alkaloids as well as eremanthin which can optimize sugar uptake in the liver. These feats could induce insulin secretion and release from cells, as well as stimulates the tissue's insulin sensitivity leading to an increase of the tissues glucose uptake, storage, and oxidation.

In another work Nascimento et al (2016b) speculated that the aqueous extract studied *Costus spicatus* has a potential hypoglycemic action which could be related to the synergic action of molecules with antioxidant profile which can enhance the secretion of insulin by the pancreas and the increase in absorption of tissue glucose level. Based on evidence from the analysis of the results, they suggested that the effect of decreasing glucose *Costus Spicatus* extract could be associated with the enhancement of insulin release from pancreatic islets and enhancing peripheral glucose utilization, thus corroborating the results obtained by Hardikar et al (2016) in a study with *Costus igneus*. Hyperglycaemia is a salient feature of poorly controlled diabetes mellitus. Rate of protein glycation is increased with hyperglycaemia leading to long term complications of diabetes. One approach of controlling blood glucose in diabetes targets at reducing the postprandial spikes of blood glucose. Perera et al (2016) points out that the methanol extracts of *Costus speciosus* (COS) leaves demonstrated *in vitro* inhibitory activities on α-glucosidase, fructosamine formation, glycation and glycation induced protein cross-linking. These results are in agreement with the hypoglycemic effect by published studies reported by Nascimento et al (2016a), as described above.

Nascimento et al (2015), reported that the extract of *Costus spicatus* features phenolic compounds with anti-hemolytic action which can be observed in more dilute samples of NaCl and saponins molecules which would be possibly related with the hemolytic effects observed at higher concentrations of saline solutions. It is known that *Costus speciosus* (Koen ex. Retz.) Sm. (crepe ginger, family Costaceae) is an ornamental plant used in traditional medicine for the treatment of inflammation, rheumatism, bronchitis, fever, headache, asthma, flatulence, constipation, helminthiasis, leprosy, skin diseases, hiccough, anemia, as well as burning sensation on urination. Al-Attas et al (2015) observed a good anti-inflammatory activity exhibited of the isolated compounds from *Costus speciosus* corroborate the usefulness of this plant in the traditional treatment of inflammation and related symptoms. These findings are complementary to those reported by Nascimento et al (2015), as well as Nascimento et al (2016a), as have been featured, with regard to the fact that possible anti-inflammatory action being allegedly related phyto compounds present in *Costus* genus, which could be related to the hypoglycemic effects as well as the anti-hemolytic effect, justifying the relevance of the potential indication of *Costus spicatus* plant in the treatment of diabetes. Diosgenin, a naturally occurring steroid saponin found abundantly in C. speciosus, is a well-known precursor of various synthetic steroidal drugs that are extensively used in the pharmaceutical industry.

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Selim and Jaouni (2015a) suggested that diosgenin isolated from *Costus speciosus* possess anticancer and apoptotic effects on cell proliferation, and therefore, can be used as pharmaceuticals drugs. It is interesting to consider that these findings could be related to the hemolytic effect described by Nascimento et al (2015).In another study Nascimento et al (2016c) suggested that the aqueous extract of *Costus spicatus* exhibit a weight management effect of the treated animals. This effect may be associated with certain mechanisms related to the phytomolecules which exhibit antioxidant and hypoglycemic action. From the chronic treatment performed with an aqueous extract of *Costus spicatus* they speculated that the referred natural extract has no adverse effects and no poses the health risk in relation to oral toxicity study.Biologic based therapies are frequently used as complementary medicines in diabetes. The practice of using household ingredients as complementary medicines is common in Brazil. Few herbal remedies and their methods of preparation have limited evidence for efficacy. In view of the frequent use by diabetic patients each needs to be documented for reference and scientifically explored about their hypoglycemic potential. In this review study was focused on the potential use of *Costus spicatus* plant as an adjunct in the treatment of diabetes due to its hypoglycemic effect well discussed in literature level. From the analysis items can be speculated that the plants belonging to the genus Costus possibly have anti-hyperglycemic activity. One can even suggest these plants exhibit molecules which induce insulin secretion and release from cells, as well as stimulate the tissue's insulin sensitivity leading to an increase of the tissues' glucose uptake, storage, and oxidation, thereby contributing to the maintainer of the weight of the body, as well as to minimize the oxidative stress, due to its antioxidant potential as suggested in the publications Nascimento et al. Picanço et al (2016) suggested that *Costus spicatus* extract could exhibit a central mechanism for pain inhibition, and may also inhibit prostaglandin synthesis. These findings corroborate the traditional administration of C. spicatus decoction to treat inflammatory disorders, including those caused by *Bothrops atrox* envenomation. These findings can be related to the presence of phyto molecules with potential antioxidant and anti-hemolytic activity as demonstrated in analysis of the possible composition of the phyto constituent present in samples from an aqueous extract of *Costus spicatus* as reported by Nascimento et al (2015).*Costus speciosus* is an important medicinal plant widely used in several indigenous medicinal formulations. Selim and Jaouni (2015b) suggested that diosgenin isolated from *Costus speciosus* possess anticancer, apoptotic and inhibitory effects on cell proliferation. These results reinforce the anti-hemolytic behavior and hemolytic support described by Nascimento et al (2015), when analyzing samples of an aqueous extract of *Costus spicatus* undergoing treatment with different saline concentrations and under tamponade.

CONCLUSION

Finally, this review highlights the need to perform pharmacological, phytochemical, toxicological, and ethnobotanical studies with *Costus spicatus*, a medicinal plant with significant therapeutic applicability which can potentially be used as an adjunct in the treatment of diabetes. From the literature review conducted we can suggest that the plant does not have toxicant activity and depending on the preparation of their phyto constituents extract can express different biological activity with antioxidant power, anti-inflammatory, anti-hemolytic and hypoglycemic as well as apoptotic effect supporting anticancer and hemolytic activities.

CONFLICT OF INTEREST

The authors declare that no competing financial interests exist.

REFERENCES

1. Al-Attas A. A., El-Shaer N. S., Mohamed G. A., Ibrahim S. R., Esmat A. (2015). Anti-inflammatory sesquiterpenes from Costus speciosus rhizomes. J. Ethnopharmacol. 24, 176, 365-74.

2. Alonso-Castro, A. J.; Zapata-Morales, J. R.; González-Chávez, M. M.; Carranza-Álvarez, C.; Hernández-Benavides, D. M.; Hernández-Morales, A. (2016). Pharmacological effects and toxicity of Costus pulverulentus C. Presl (Costaceae). J Ethnopharmacol. Mar 2;180:124-30.

3. American Diabetes Association. (2009). Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. Jan; 32(Suppl 1): S62–S67.

4. Antoniolli, A. R.. (2007). Avaliação do Potencial Terapêutico de Plantas Medicinais com Atividade Anti-hipertensiva e Antidiabética utilizadas no Povoado Colônia Treze em Lagarto/SE e Implantação de uma Farmácia Viva, Cratos, Sergipe.

5. Badke, M. R.; Budó, M. L. D.; Alvim, N. A. T.; Zanetti, G. D.; Heisler, E. V. (2012). Popular knowledge and practices regarding healthcare using medicinal plants. Text Context Nursing, Florianópolis, 21(2): 363-70.

6. Brasil. (2006). Ministério da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Assistência Farmacêutica. A fitoterapia no SUS e o Programa de Pesquisa de Plantas Medicinais da Central de Medicamentos / Ministério da Saúde, Secretaria de Ciência, Tecnologia e Insumos Estratégicos, Departamento de Assistência Farmacêutica. – Brasília: Ministério da Saúde,

148 p.

7. Damasceno Adriana De Assis. (2005). Levantamento Etnobotânico de Plantas do Bioma Cerrado na Comunidade de Martinésia, Uberlândia , M.G.

8. Engelstoft, M. S.; Schwartz, T. W. (2016). Opposite Regulation of Ghrelin and Glucagon-like Peptide-1 by Metabolite G-Protein-Coupled Receptors. Trends Endocrinol Metab. Jul 27.

9. Gasparri S. (2005). Estudo da atividade antioxidante mutagênica/antimutagênica induzida pelo extrato vegetal da *Costus*, Dissertação (Mestrado – Área de concentração em Diagnóstico Genético e Molecular) - Universidade Luterana do Brasil, Canoas, 78.

10. Guyton, A. C.; Hall., J. E. (2011). Guyton & Hall - Tratado de Fisiologia Médica - Editora: ELSEVIER / MEDICINA NACIONAL.

11. Hardikar, M. R.; Varma, M. E.; Kulkarni, A. A.; Kulkarni, P. P.; Joshi, B. N.(2016). Elucidation of hypoglycemic action and toxicity studies of insulin-like protein from *Costus igneus*. Phytochemistry. Apr;124:99-107.

12. Internacional Diabetes Federation, IDF. (2009). Diabetes Atlas - 4th Edition.

13. Martins, N. L. P. (2006). Comparative analysis of skin healing with the intraperitoneal use of aqueous extract of *Orbignya phalerata* (rubs) controlled study in rats. ORIGINAL ARTICLE, 66, Brazilian Surgical Acta, Vol 21 (Supplement 3).

14. Nascimento, C. C. H.C.; Azevedo, L.A.C.; Peixoto, G.; Vieira, T. O.; Camacho, A. C. L. F.; Oliveira, J. F. F.; Gomes, M.L.; Nascimento, S. F.; Pinto, P. R.; Barreto, A.S.; Diré, G. F. (2015). Spectrophotometric And Hemolytic Analysis Of An Extract Of *Costus Spicatus*. European Journal Of Biology And Medical Science Research., March; 3(1): 29-58.

15. Nascimento, C.C.H.C.; Azevedo, L.A.C.; Camacho, A. C. L. F.; Oliveira, J. F. F. ; Gomes, M. L.; Nascimento, S. F.; Vasconcelos, S. D. D. De; Nogueira, R. I.; Barreto, A. S.; Diré, G. F. (2016a). Analysis of

hypoglycemic effect of an aqueous extract of *Costus spicatus* on F1 mice subjected to hyperglycemic diet. International Journal of Advanced Research in Biological Sciences, 3(2): 99-107.

16. Nascimento, C.C.H.C.; Armada-Dias, L.C.; Azevedo, L.A.C.; Camacho, A.C.L.F.; Oliveira, J.F.F.; Gomes, M.L.; Nascimento, S.F.; Vasconcelos, S.D.D.De; Nogueira, R.I.; Barreto, A.S.; Diré, G.F. (2016b). Study Of The Biological Effect Of An Aqueous Extract From A Medicinal Plant (*Costus Spicatus*) F1 Mice Treated With Hyperglycaemic Diet. Internacional Journal Research Biosciences., 5(2): 30-39.

17. Nascimento, C. C. H. C.; Vasconcelos, S. D. D. De; Nascimento, S. F.; Oliveira, J. F. F.; Nogueira, R. I; Barreto, A. S.; Diré, G. F. (2016c). Analysis of Measurement of Weight of Animals Treated With a Freeze-dried Aqueous Extract of *Costus spicatus*. World Journal of Pharmaceutical and Medical Research, 2016,2(4), 190-195.

18. Organização Pan Americana da Saúde, (OPS). (2005). Visão Geral, Canadá.

19. Pereira, H. K.; Premadasa, W. K.; Poongunran, J. (2016). α-glucosidase and glycation inhibitory effects of *Costus speciosus* leaves. BMC Complement Altern Med. Jan 5;16:2.

20. Picanço, L. C.; Bittencourt, J. A.; Henriques, S. V.; Da Silva J. S.; Oliveira, J. M.; Ribeiro, J. R.; Sanjay, A. B.; Carvalho, J. C.; Stien, D.; Silva, J. O. (2016). Pharmacological activity of *Costus spicatus* in experimental Bothrops atrox envenomation. Pharm Biol. Jun 16:1-8.

21. Quintans Júnior, L. J.; Santana, M. T.; Melo, M. S.; De Sousa, D. P.; Santos, I. S.; Siqueira, R. S.; Lima, T. C.; Silveira, G. O.; Antoniolli, A. R.; Ribeiro L. A.; Santos, M. R. (2010). Antinociceptive and anti-inflammatory effects of *Costus spicatus* in experimental animals. Pharm Biol. Oct; 48 (10):1097-102.

22. Roche. (2003). Copyright by Diabete.com.br - Diabete® 1998-2003 - Direitos Reservados, Brasil.

23. Selim, S.; AL Jaouni, S. (2015a). Anti-inflammatory, antioxidant and antiangiogenic activities of diosgenin isolated from traditional medicinal plant, *Costus speciosus* (Koen ex.Retz.) Sm. Nat Prod Res. Jul 29:1-4.

24. Selim, S.; Al Jaouni, S. (2015b). Anticancer and apoptotic effects on cell proliferation of diosgenin isolated from *Costus speciosus* (Koen.) Sm. BMC Complement Altern Med. Sep 2;15:301.

25. Tsuneki, H.; Sasaoka, T.; Sakurai, T. (2016). Sleep Control, GPCRs, and Glucose Metabolism. Trends Endocrinol Metab. Jul 22.

26. Wheeler, S. E.; Lee, N. Y. (2016). Emerging Roles of Transforming Growth Factor β Signaling in Diabetic Retinopathy. J Cell Physiol. Jul 29.

27. World Health Organization, (WHO). (2007). World Health Report, 1st edition.