

# **ACTION OF CYANOGENIC SUBSTANCES AND MAGNETIC FIELD IN THE REDUCTION OF NEOPLASMS: AN INTEGRATIVE LITERATURE REVIEW**

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## **Abstract**

*Cancer treatment has been constantly improved to have the least possible harm to the patient. New therapies are being researched, many of them having as the object of scientific-academic and pharmacological investigation the use of cyanogenic plants and their antitumor chemical compounds that can bring benefits to human health, having the potential to be associated with the magnetic Field and thus achieving a better benefit and with reduced adverse effects in cancer treatment. This study aimed to review the effect of cyanogenic substances and the magnetic Field on tumor evolution in the literature. The integrative literature review was in the EMBASE, PUBMED, LILACS, VHL, SCOPUS, and MEDLINE databases. A final sample of 14 scientific articles, published from 2011 to 2020, was obtained, highlighting that cyanogenic substances and the magnetic Field can help reduce tumors. The most common studies were on the magnetic Field, and their research was mainly carried out in vitro, with the frequency of 50hz that stood out over other frequencies. Among the cyanogenic substances, the most prevalent was amygdaline, with the most used dosage of 10mg/ml. It was possible to conclude that both the magnetic Field and cyanogenic substances can reduce tumors.*

**Keywords:** Neoplasm, Magnetic Field Therapy, Amygdaline.

## **Introduction**

It is public knowledge that mentions about the occurrence of neoplasm's (cancers) are a Constant in the history of humanity. Cancer is one of the main public health problems in the world, being among the four leading causes of premature deaths in the vast majority of countries (BRAY et al., 2018). However, Teixeira and Fonseca (2007) report, technical, political and administrative problems still prevail in the Field of

health, which, each in its own way, hinder research and treatment efforts regarding searches related to the possibilities of cure of neoplastic diseases. The stratospheric expenditures spent on the many Technologies employed impacts on the results – and the effort to obtain them; which fatally reverberates and negatively influences the therapeutic-preventive processes, limiting (or making impossible) the proper treatment of a wide range of cancers. These obstacles go beyond the stricto sensu medical-pharmacological sphere, entering the sociopolitical field and making the issue of combating neoplasm's a social problem of prevention and public health (TEIXEIRA; FONSECA, 2007).

With regard to epidemiology, occurrence, hospital morbidity and mortality are configured as strategies that epidemiological surveillance uses to monitor and control the incidence of cancer. These strategies provide an analysis of the occurrence, distribution and evolutionary development of neoplasms. This information, regarding the epidemiological profile of the various types of cancer, is essential for the elaboration of political and sanitary mechanisms aimed at controlling cancer diseases worldwide (INCA 2021).

The monitoring of cancer cases allows the construction of more efficient preventive approaches, so much so that, according to the American Cancer Society (ACS), in the period between 1991 and 2018 there was a significant drop in overall cancer mortality, and the figures show a 31% reduction in incidence, which means that 3.2 million deaths from cancer were avoided in this period (SIEGEL; MILLER, 2015). In this sense, in Brazil and in the world, it is particularly relevant to the indicators and the forms adopted in their elaboration; since the indicators are nothing more than numerical data derived more frequently from the Cancer Records and the Mortality Information System (SIM/MS) (INCA 2021).

In Brazil, the estimate for each year of the triennium 2020-2022 indicates that 625, 000 new cases of cancer Will occur (450,000, excluding cases of non-melanoma skin cancer). Non-melanoma skin cancer Will be the most common (177, 000), followed by breast and prostate cancers (66, 000 each), colon and rectum (41, 000), lung (30, 000) and stomach (21, 000) (INCA 2021). Also according to INCA (2021), the trend for 2030 indicates that there are 26 million new cases and 17 million cancer deaths worldwide. The figures described are explained by the population's population growth and aging process, especially in less developed regions (BARBOSA et al., 2015).

The treatment of cancer aims at the elimination of the tumor, by means of medication and/or the complete removal of the tumor through surgery, when the clinical-pathological condition of the patient allows. For this to occur, there are different procedures to be addressed for successful treatment, and surgery, radiotherapy, hormone therapy, immunotherapy, guided therapies and chemotherapy can be described. With these local treatments, one third of patients achieve cure while the other cases occur the appearance of micro metastases, which indicates a more systematic approach to the disease (ALMEIDA et al., 2005). The Constant search for substances that are toxic only to cancer cells, to AID in the advancement of chemotherapy, has become increasingly Constant. In this sense, it has been observed that compounds containing nitril do not present toxic effect while they are in intact form, since when they are passed through an enzymatic digestion process, they end up becoming toxic. However, there are some cyanogenic compounds– such as Linamarina and Amygdaline – that have therapeutic effects and have been used in the treatment of cancer (RAMALHO, 2010; MOSAYYBEBI et al., 2020).

The interest in the use of plants and their plant derivatives for the purpose of treating and preventing diseases has been growing, being of great interest to the pharmaceutical industry, in view of this is essential

the study of medicinal plants, evaluating their effectiveness through toxicological and pharmacological tests (COSTA, 2018). Cyanogenic plants contain cyanide acid (HCN), being a cyanide, is a colorless, volatile and toxic liquid and when bound to carbohydrates they name cyanogenic glycosides (MOSAYYEBI et al., 2020).

Cyanides can be absorbed by the gastrointestinal mucosa; these cyanide Sais at low ph when absorbed by the stomach releases cyadidic acid. Hydrocyanic acid has low molecular weight, which is soluble in water and lipids having its rapid absorption. When cyanide is absorbed, it easily enters the cell membranes by difference in concentration, and within the cells cyanide compromises oxidative phosphorylation. (RUFINO et al., 2014).

Advances in medicine in various fields of knowledge have led to progress never seen before. In 1820, the Danish physicist named Hans Christian Oersted observed that an electric current as it traversed the turns of a solenoid produced a magnetic Field around it and consequently the North Pole and the South Pole appeared on the opposite sides. This magnetic Field generated by the electric current was named electromagnetic Field to differentiate from that produced by magnetite magnet (MUSSOI, 2005; HAYT; BUCK, 2011).

A magnetic Field is defined as a region of space in which the electrical charges in circulation are determined by the action of a magnetic force, whose capacity can alter its trajectories. Thus, roughly speaking, one can understand the magnetic Field as the result of the activity of electrical charges, such as a wire that conducts electric current; or the contingent displacement of subatomic fragments, such as electrons (BUCK, 2011). Another relevant proof is that the electromagnetic Field is not Constant, but its intensity depends directly on the intensity and frequency of the electric current that runs through the turns, the physical dimensions of the solenoid and the magnetic permeability of its nucleus. This solenoid was called an electromagnet, being easily constructed with copper wires and having as another great advantage to allow the control of the intensity and frequency of the electromagnetic Field and consequently of magnetic force (HAYT; BUCK, 2011).

Thus, the execution of this dissertation with Integrative Review – Action of Cyanogenic Substances and magnetic Field – in the reduction of Neoplasm's is justified, since it is increasingly necessary the accumulation, and dissemination, of scientific-academic information about the various efforts made by researchers in the search to resolve human suffering caused by cancers worldwide.

## **2.1 Cancer (Carcinogenesis)**

Cancer is one of the oldest diseases in the world. In ancient Egypt, approximately 3000 a.C., those Who were dedicated to researching diseases in an attempt to find treatment had already identified diseases that, by the characteristics reported by these individuals, could most likely be categorized as cancer. The name of the disease originates from the Greek Word Karkinos or "crab"; name used by Hippocrates more or less in the year 400 a.C. The Word chosen was because Hippocrates found similarities between the tumors he studied and the blood vessels surrounding the crab when it has its paws (pereopods) scattered in the sand (MUKHERJEE, 2012).

From the Greek was also pinched another Word to designate cancer: Onkos; term generally used to designate a kind of shapeless mass that resembled a burden – this is due to the cancer being considered at the time as a weight carried by the body.

Historically, one of the oldest records, considered the first to be made regarding cancer and its visible characteristics, was identified is an Egyptian papyrus from the 7th century a.C. Papyrus is attributed to the Imhotep physician and was only translated in 1930. Through this historical document, a series of technical knowledge and reports on various diseases that affected the Egyptian population at the time, among which there was the mention of the prominent masses that appeared in the chest of the sick and spread throughout the body (MUKHERJEE, 2012).

Thus, it is evident that cancer has been a disease present in humanity for several centuries. However, what the old documents allow to be seen are the possibilities of cancer being a Constant in the history of human diseases; and only in Europe in the mid-eighteenth century were deaths whose causes were attributed to cancer and the complications that occurred from it. Since then, episodes involving cancer as a cause have increased exponentially, with high mortality rates in several countries. This trend has been accentuated after the 19th century, with the emergence of industrialization.

Cancer has been described as the biggest public health problem in the United States of America and many other parts of the world (SIEGEL; Miller, Miller, "MILLER". JEMAL, 2015). The overall incidence for 2020 Will be 17, 113, 588 new cases (FERLAY et al., 2013). Research around the world shows a dramatic increase in the number of cancer cases. What would be causing this upsurge?

Suspensions often fall on the numerous changes in sociocultural reality in recent decades, in which the rural exodus has been identified in various parts of the world, leading huge population contingents to migrate to urban areas. In this change, sedentary lifestyle and poor diet – based on industrialized ones – have contributed to the increasing number of cancer cases (GAROFALO et al., 2004). In addition to these transformations in lifestyle, according to Garofalo et al. (2004), a greater longevity of the world's population. With the highest life expectancy, the occurrence of chronic-degenerative diseases, such as cancer, diabetes and heart diseases, increase exponentially.

Although it seems a unique type of disease, cancer is the generic name for a set of more than 100 different types of diseases – having in common the abnormal growth of deficient cells with the potential to reach healthy tissues of the affected organism. The etiology of cancer is multifactorial, involving combinations with several variables such as genetic, environmental and lifestyle factors of individuals, such as smoking and poor diet. All these factors can have joint or separate action in the process that gives rise to cancer cells. Given the diversity of possibilities of origin, multiple and multifaceted are also risk factors, always depending on the organ and/or tissue at the disease (INCA 2019).

Among the various types of cancer, we highlight the breast, prostate, skin (melanoma), colorectal, lung, cervix, stomach, head and neck, thyroid, ovary, to name some of the most prevalent.

According to information from Bray et al. (2018), citing worldwide estimates of cancer incidence worldwide, there were only a total of 17 million new cases of cancer in 2018 (except 1 million cases of non-melanoma skin cancer), leading to death of 9.5 million people. According to the data collected by Bray (et al., 2018), the most prevalent type of cancer worldwide are lung and breast cancer (2.1 million, respectively), colon and rectum (1.8 million) and prostate cancer (1.3 million) (BRAY et al., 2018).

Overall, there was a higher occurrence in men (9.5 million), figures that represent 53% of new cases recorded, with a slightly lower incidence in women, with 8.6 million (47%) of new case records. In this 2018 estimate, men were more affected by lung cancer (14.5%), prostate (13.5%), colon and rectum (10.9%), stomach (7.2%) and liver (6.3%). In the case of women, the types of cancer with the highest incidence were breast (24.2%), colon and rectum (9.5%), lung (8.4%) and cervix (6.6%) (BRAY et al., 2018).

Cancer can be described as the disease that causes the most fear in society due to its high mortality, physical pain and psychological-emotional suffering – both of the patient and of his family and friends. When we refer to the term cancer, we must keep in mind that it refers to the term neoplasia, specifically malignant tumors (ALMEIDA et al., 2005).

The process of carcinogenesis, which leads to the emergence of cancers, is presented as a result of the biological malfunction of cells. Cells that are sick multiply disorderly and completely modify the structure of the tissue, causing a number of problems to the health of the affected organism. As these cells divide very quickly, the level of aggressiveness of it becomes much higher and with this become very difficult to control causing, thus, the formation of malignant (and also benign) tumors or neoplasm's (ALMEIDA et al., 2005; BRAZIL, 2011; SURESH, 2007).

## **2.2 Metastasis**

The Word metastases originates from the Greek language (Meta = beyond; stasis = stop) and was primarily used to serve the Humoral Physiological Theory, whose performance lasted between the years 400-500 BC. The Humoral Physiological Theory argued that the harmony of body homeostasis could be achieved through the perfect balance between the four organic humors, yellow bile, blood, Black bile and phlegm (SIM; FRASSICA, 1998).

Neoplasm's considered benign differ from malignant ones, since the former present organized development, usually slowly; characterized by clear limits of action in the body. In this type of carcinogenic process, cancer cells do not invade surrounding tissues, nor advance to the stages known as metastases – migration through the bloodstream or lymphatic of elements considered pathological (viruses, bacteria, parasites and other cancer cells), arising from an initial lesion). As examples of benign tumors, we have fibroids and lipomas (INCA 2021).

The process of metastasis does not usually, in most cases, give rise to symptoms that have not yet manifested symptoms, that is, they do not present differentiated symptoms; but when this occurs, the intensity and symptomatic typology vary according to the region reached. According to Meohas et al. (2005), the symptoms, when metastasis occurs in the bones, are, in general, recurrent fractures and pains in the affected bone; when the affected region is pulmonary, it is usually seen in patients feeling short of breath and consequent and marked discomfort and difficulty breathing; if the area of the body affected by metastasis is the brain, sick individuals often report severe and recurrent headaches; if the organ is the liver, symptoms appear as pain and swelling in the abdominal region, yellowish eyes and skin (D'ANGELICA, 2007; GOMES et al., 2014).



In the case of bone neoplasm's, tumors have a low incidence (about 1%) when compared to other types of cancer. Although they can be affected by numerous types of cancer, the bones have a higher prevalence in the following types: Osteosarcomas, Ewing tumors and chondrosarcomas (MEOHAS et al., 2005).

The treatment takes place through surgeries, chemotherapy and radiotherapy, and in most cases the patient is initially submitted to chemotherapy; then, the tumor is removed by surgical procedure and the region is again submitted to chemotherapy sessions. If the tumor under treatment is Ewing's, radiotherapy after surgery is used if necessary. This therapeutic strategy can prevent the affected part from being amputated, which is suggested when the procedure does not mean immediate risk of death to the patient. However, if amputation cannot be avoided, there is the possibility of using reconstructive measures of the affected area, or even the use of prostheses (OLIVEIRA; MELLO; PASCHOAL, 2016).

Regarding lung cancer, its categorization takes place in two groups: carcinomas whose cells are considered small (oat cell carcinomas) and non-oat cell carcinomas. In the second group, the cancer called adenocarcinoma is located; whose characteristics are the presence of squamous cells and large cell carcinoma (INCA 2021).

In medical jargon, the expression oat cell designates a specific subtype of lung cancer, whose most patent and recurrent aspects are rapid development, potential for great irradiation by the body and recurrent brain uptake. Despite the fact that the treatment presents highly satisfactory responses, the cure rate of this type of cancer is very low, increasing the number of deaths as a result of its performance in the body (INCA, 2021).

Cancer treatment aims at complete tumor removal and for this to occur, there are different procedures to be addressed for successful treatment, and surgery, radiotherapy, hormone therapy, immunotherapy, guided therapies and chemotherapy can be described. With these local treatments, one third of patients get the cure; while in other cases there is the appearance of micro metastases, which indicates a more systematic approach to the disease (ALMEIDA et al., 2005).

### 2.2.1 Cyanogenic substances

We can term cyanogenic plants as those that have cyanogenic glycosides, which are found in many plants, especially in rosaceous, legumes, grasses and Arabidopsis. Two groups of metabolisms produced by the plant, cyanogenic glycosides and cyan lipids, release cyanide acid (HCN) through hydroxylases, with cyanogenic glycosides being the most important, with more than 25 types identified. Some examples can be cited, such as tonsil in, durrin and linamarin (CÂMARA; DALCIN; SOTO-BLANCO, 2014).

The interest in the use of plant derivatives for the treatment and prevention of diseases has been growing a lot in recent times, having a great interest of the pharmaceutical industry, being essential and important the study of medicinal plants, to evaluate their efficacy through toxicity and pharmacological tests (COSTA, 2018).

Much of this interest in the therapeutic-curative potential of plants has been shared by Brazilian health authorities, which can be verified in the effort to insert into the Unified Health System (SUS) of the country a national list of medicinal plants, known as RENISUS (National Relationship of Medicinal Plants of Interest to the Unified Health System). The initiative to organize the multiple knowledge about plants and

their potential stems from the recognition of popular medicine – and its various traditional knowledge – whose use has been increasingly the object of studies by the pharmacological industry, both in the Brazilian and international spheres (BRASIL, 2009; BALICK, BALICK. COX, 1997; COELHO-FERREIRA, 2000).

Among the studies carried out with plants and their effects as an object, some that aim to discover possible therapeutic potentials for cancer treatment stand out. As one of the forms of tumor cell regression, cyaniding acetone (CA) has been used. It is only possible to perform this approach because of its molar equivalent of cyanide that is anchored in neoplastic cells and these cannot eliminate cyanide due to the reduction of sulphane compound (RAMALHO et al., 2013; RAMALHO; AYDOS; CEREDA, 2010).

According to Essers (1993 apud RAMALHO; AYDOS; CEREDA, 2010), cyanide is commonly found in the environment and both men and animals can be exposed through different forms found such as in water, plastics, acrylics, cigarette smoke and cyanogenic plants. Cyanide inhibits cellular respiration and acts on enzymes that contain iron (Fe), preventing oxygen (O) consumption. When ingested it can bind to the iron of hemoglobin, interrupting the transport of oxygen from the blood (FURTADO et al., 2007).

In another study, it can be observed that the influence of cyanide, released by Acetone Cyanidrin (CA), on the treatment of Ehrlich tumor demonstrated that cyanide promoted an increase in necrosis and inhibited tumor growth when compared to the control group, again proving the difficulty of tumor cells in eliminating cyanide (RAMALHO et al., 2014).

Tonsil in, can also be known as laetrile is a cyanogenic glycoside that belongs to the family Rosaceous, also known as vitamin B17, not being toxic, but produces a substance the HCN that at the dosage of 4g for 15 days can generate toxicity to the human body. Tonsil in can be isolated in almonds, cherries, peaches and plums and have many advantages because it is antitumor, antipyretic, antiasthma tic and improves the immune system (QADIR; FATIMA, 2017).

## **2.3 Magnetic Field**

In 1820, the Danish physicist named Hans Christian Oersted observed that an electric current as it traversed the turns of a solenoid produced a magnetic Field around it and consequently the North Pole and the South Pole appeared on the opposite sides. This magnetic Field generated by the electric current was named electromagnetic Field to differentiate from that produced by magnetite magnet (MUSSOI, 2005; HAYT; BUCK, 2011).

Another relevant proof is that the electromagnetic Field is not Constant, but its intensity depends directly on the intensity and frequency of the electric current that runs through the turns, the physical dimensions of the solenoid and also the magnetic permeability of its nucleus. This solenoid was named Electromagnet and was easily constructed with copper wires and had as another great advantage to allow the control of the intensity and frequency of the electromagnetic Field and consequently the magnetic force (HAYT; BUCK, 2011).

The magnetic Field varies around a frequency called Hertz and the size of the wave. The lower outer of the frequency spectrum is represented by the direct current or static Field. The upper end frequently above 10

Hz comprises ionizing radiation, x-rays, gamma rays and ultraviolet light (MARCILIO; HABERMANN; GOUVEIA, 2009).

Modern society is constantly being exposed to various types of magnetic fields during its Day, be they low frequency, where its frequencies are 3 to 30 Hz, or those of super low frequency; where their frequencies are presented from 50 to 60 Hz and very low frequencies that can be quantified from 3 to 30 KHz (GYE; PARK, 2012).

In recent times, much has been studied about the interaction of magnetic fields with living cells and organisms. The advance of experimental techniques and the Eergeny of new magnetic models resulted in the development of new approaches in intracellular and molecular levels (ZABLOTSKII et al., 2016).

The interconnection between the extremely low frequency magnetic Field and the human body is weak, not being able to destroy chemical bonds and are known as non-ionizing radiation (WHO, 2008; AHLBOM; FEYCHTING, 2003). However, this low capacity for action of ionizing radiation has been disputed, because there is the possibility of other forms of magnetic fields interacting with individual cells to generate such changes, as suggested by Lechter (1991) and Becker (1972).

Other researchers, such as Lai & Singh (1997), consider that even though the 60 Hz EMFs do not have high ionization capacity, being considered as non-ionizing, that is, they would be unable to penetrate, by vibration, the DNA chains; there is the possibility that the Joule Effect, developed in the irradiated organism, Will be able to promote a similar rupture. Marino and Morris (1999) warned, as early as 1999, of the need to carry out studies that had the EMC as an object, nod. For the authors in question, the EMC is considered a biological stressor and, due to the increasing levels of stress in modern populations, chronically stressed, the probability of greater emergence of diseases is increasingly present (MARINO; MORRIS, 1999).

The electromagnetic Field could retain the drug and thus concentrate the effect only on the affected organs in order to restrict collateral damage that would aggravate the condition. The second possibility would be the release of the active ingredient of the drug only in the affected organs and in tumors under the action of the electromagnetic Field. The third possibility would be to favor that different drugs combine properly under the action of the electromagnetic Field in a specific place of the body.

The fourth possibility would be to individually test distinct electromagnetic fields that present distinct intensities and frequencies to monitor those Who Interact adequately and conveniently with the disease. The fifth possibility would be to simultaneously combine the effects of distinct electromagnetic fields in order to provoke the desired interaction with the affected organ. The sixth application would be to insert into the bloodstream magnetic nano particles that would aggregate the drugs and could produce the equivalent effect in the disease (HUGHES et al., 2007; Gye; PARK, 2012; KOZISSNIK et al., 2013).

When one thinks of the toxicity of the cell mechanism induced by the electromagnetic Field, an increase in free radicals and calcium (Ca) can be interfered with the effect of the magnetic Field, leading to inhibition of cell growth, DNA breakdown and protein changes (GYE; PARK, 2012).

In a study conducted by Koh et al. (2008), it was observed that the continuous 60Hz effects of sinusoidal magnetic field in three types of prostate cancer were understood that there was an inhibition of tumor growth and considerably promoted apoptosis and cell cycle arrest. So IF we associate the 60HZ magnetic



Field with chemotherapy or radiotherapy, we may have a good technique with conventional prostate cancer treatments.

### **Three of them. METHODOLOGY**

Literature reviews, or bibliographic reviews, are divided into three: narrative, systematic and integrative. The definition of the type to be used depends on the method chosen for the preparation of the ongoing study, and it is at the discretion of the researcher to list the one that Best meets the needs of his research (MARCONI; LAKATOS, 2010).

Regarding the integrative review, Whitemore and Knafl (2005 apud GRUPO ANIMA, 2014, p. 6) explain that the "integrative term originates from the integration of opinions, concepts or ideas from the researchers used in the method". Botelho, Cunha and Macedo (2011, p.133 apud GRUPO ANIMA, p. 6) point out that the integrative review, as a method of data collection, can be "incorporated into the research carried out in other areas of knowledge, in addition to the areas of health and education", in view of the potential that the technique harbors in order to make possible the organization of knowledge produced by science in its various modalities.

The integrative review allows researchers a better approximation "of the problem they want to appreciate, tracing an overview of their scientific production to know the evolution of the theme over time and, with this, visualize possible research opportunities" (GRUPO ANIMA 2014, p. 6).

According to Souza, Dias and Carvalho (2010), the Integrative review involves three phases: the first is the phase of the elaboration of the right-line question, which is, according to the cited authors, "the most important phase of the review". It is at this stage that it is established which studies Will be part of the analysis of the theme under consideration, as well as what strategies Will be adopted to raise the most important points of each study to be evaluated.

The second phase involves the search or sampling in the literature, which should explore databases in a "broad and diversified way, contemplating the search in electronic databases, manual search in journals, the references described in the selected studies, contact with researchers and the use of unpublished material" (SOUZA; DAYS; CARVALHO, 2010, p. 104).

The sampling criteria need to ensure the representativeness of the sample, being important indicators of reliability and reliability of the results. The ideal approach is to include all studies found or their randomized selection; however, IF the two possibilities are unfeasible by the number of papers, the inclusion and exclusion criteria of articles should be clearly established and discussed. Thus, the determination of the criteria should be performed in accordance with the main question, considering the participants, the intervention and the results of interest (SOUZA; DAYS; CARVALHO, 2010, p. 104).

The third phase consists of extracting data from selected articles. Therefore, it is necessary to use previously structured instruments, which are able to ensure that the computation of the relevant data is adequately extracted, avoiding and/or minimizing, thus, the possibility of having problems in the transcription. Another positive aspect of this third phase of the integrative review is to ensure accuracy in the measurement of the information prospected and analyzed, in addition to serving as a Record (SOUZA; DAYS; OAK, 2010).

Because it is an integrative review, it analyzes relevant research to support decision-making and improvement in clinical practice and makes it possible to synthesize the current state of knowledge of a specific subject, allowing finding gaps in the literature. Thus, the integrative review has the potential to reduce barriers in care practice (GALVÃO; SAWADA; TREVIZAN, 2004).

For the construction of the integrative review, a methodological protocol was used, consisting of seven phases (GALVÃO; SAWADA; TREVIZAN, 2004).

**First phase:** preparation of a protocol to conduct the research. Inclusion criteria were: Experimental studies, cross-sectional studies, cohort, control case, randomized clinical studies addressing malignant neoplasia published in English, Portuguese, Spanish and Russian, published from 2011 to 2021.

The search and selection of the articles were carried out by two researchers independently. After searching for the articles, all identified citations will be uploaded by email and entered in the Intelligent Systematic Review (RAYYAN) and duplicates removed.

Rayyan was developed through the Qatar Computing Research Institute, funded by the Qatar Foundation, a non-profit organization that supports community education, science, and research and development initiatives in Qatar. It is fully web-based, with offline compatibility through your application. Users can start and/or participate in an unlimited number of revisions is actually designed only to help in referral screening. It is a minimalist approach, placing more logistics and workflow load on the users themselves (KELLERMEYER et al. 2018). The results of the search and inclusion process of the study will be reported in full in the integrative review and presented according to the preferred reporting items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (PAGE et al. 2021).

**Second phase:** Identification of the problem and the formulation of the research question. For this we used the PICO strategy (CUNHA, CUNHA, ALVES, 2014).

**P** - Patients or animals in the treatment of neoplasm's;

**I** - Use of cyanogenic substances and magnetic Field for the treatment of neoplasms

**C** - Patients and animals that underwent conventional treatment for neoplasms.

**O** - Reduction of tumors and adverse effects.

In this sense, the question was defined: What are the effects of cyanogenic substances and magnetic Field on tumor evolution?

**Third phase:** Search for studies in journals of published material. The following databases were used: PUBMED (National Center for Biotechnology Information), VHL (Virtual Health Library), LILACS (Latin American and Caribbean Literature on Health Sciences) and SCOPUS. The descriptors were combined by means of the Boolean operators "AND" and "OR". For the search, the descriptors controlled and uncontrolled were used, having as research platforms: Pub med, VHL, Lilacs and Scopus.

**Fourth phase:** Selection of studies, guided by inclusion criteria defined in the first phase, and literature review studies, congress abstracts, editorials, comments, case series, case reports were excluded. At this stage, a preliminary reading of the titles and abstracts of the articles found was performed.

**Fifth phase:** consists of the critical evaluation of the articles found. At this stage, the articles included in the fourth phase were read in full.

**Sixth phase:** The extraction of the data contained in the studies included individually. For this, an instrument and a database were elaborated to help conduct the collection of information and reduce errors in transcription and avoid excluding relevant data.

**Seventh phase:** aims to synthesize the data resulting from each selected study. Thus, data analysis was done descriptively.

## **4:RESULTS AND DISCUSSION**

The articles were found in the Pub Med, VHL, Lilacs, Medline and Scopus databases, out of a total of 24,398 articles, which were excluded by duplicate 1371 articles. Among those left were excluded by title 22667, which presented clear inadequacy to the theme. After reading the abstract, 360 articles were qualified, and the abstracts were read independently by 2 team researchers. Of these articles that were separated for full reading, 59 were included.

Of the 59 articles selected for full reading, 11 articles were excluded because it was a literature review, 10 articles were excluded because they had more than 10 years of publication, and 24 articles were excluded, because during their reading in the integral showed that they did not refer to the theme of the dissertation. Thus, in the end, 14 articles were adapted to the work that were read in full and that met all inclusion criteria for the work, all of which were published in the English language.

The database that prevailed in the research was Pub med with 9 articles, followed by the VHL with 3 articles and finally from Scopus with 1 article, they were later separated as to the type of study, 13 of which were experimental studies and 1 of randomized studies.

Regarding the types of cancer presented in the selected studies, the most highlighted were Erlich's tumor, prostate cancer, glioblastoma and lung cancer followed by breast cancer, bladder cancer, kidney cancer, melanoma, nephroblastoma, neuroblastoma and finally adenocarcinoma.

Cyanogen glycosides are substantiated half of sugar and half of  $\alpha$ -hydroxynitrile-typeaglycone and are found in many plants one of them would be rosaceous. When is in the presence of  $\beta$ -glycosidase. Hydrogen cyanide is produced by cyanogenic glycosides that cause toxicity (MOSAYYEBI, et al. 2020).

The magnetic Field is an electric current that when going through the spirals of a solenoid produces a Field, varying in a frequency called Hertz (MUSSOI, 2005 and MARCILIO; HABERMANN; GOUVEIA, 2009). The main objectives found were the reduction of neoplasia and the increase in the proposed treatment in cell permeabilization. El-Bialy and Rageh (2013) observed in their study that 20% of mice treated with extremely low frequency magnetic Field exposure had an increase in the quantity of damaged cells.

El-Masry et al. (2020), found that the use of vitamin B17 may be beneficial for the treatment of Ehrlich's tumor, because vitamin B17 makes tumor cell apoptosis. Crocetti et al. (2013) reported that the use of the magnetic field of frequency and ultralow intensity at 20 Hz frequency and with 3 mT of intensity for 60 minutes daily increased the time and gained a greater significance after 3 consecutive days of exposure in tumor reduction.

After reading the articles, it was observed that 8 selected articles were related to the treatment with magnetic field and 6 articles were related to the treatment with cyanogenic substances.

Data cited above corroborate with Mani et al. (2019) and Gellrich et al. (2018) report in their studies that therapy with cyanogenic substances reduced chemo tactic activity, tumor cell ideation and migration and that the magnetic field increases antitumor activity and increase the effectiveness of chemotherapy by opening the tumor-blood barrier.

When the exposure of tonsillin in tumor cells was verified, there was a concentration-dependent reduction in the number of tumor cells, and no sign of x-ray was demonstrated by the trip an blue test (MAKAREVIC' et al, 2014). Corroborating with Makarevic' et al. (2014), Ramalho et al. (2014), reported in his study that cyanidrin acetone, which is a cyanogenic substance, has a strong inhibiting action on tumor growth.

Yuan et al. (2018), observed that in the cell lines of neforblastoma and neuroblastoma, including G401, CHLA255 and N2a, after exposure to the magnetic field for 2 hours/day, the viability of the tumor cell decreases significantly after 2 days of magnetic field application. Confirming what was described, Vadalá M. et al. (2016), in his study, in his study, magnetic field therapy in tumor cell lines such as pheochromocytoma-derived (PC12), breast cancer (e.g., MCF7, MDA-MB-231 and T47D), and colon cancer (SW-480 and HCT-116) showed proliferative inhibition and rupture of the fibrotic spindle.

Makarević et al. (2016), observed in their study that tumor exposure of tumor cells PC3, DU-145 and LNCaP of the cell line of prostate cancer, tonsil in several dosages, led to a reduction in the concentration of tumor cells, with more prominent effects on the concentration of 10mg/ml of tonsil in. We can quote Shi et al. (2019), which reported in its review that tonsil in exerted antitumor effect on tumor cells of human colon cancer, where the cDNA result showed a significant difference in the expression of SNU-C4 cells after treatment at a dose of 5mg/ml for 24 hours.

The adverse effects of the selected articles were difficult to find, since most studies were conducted in vitro. Of the 6 (100%) articles presented in Chart 3, 4 (66.7%) of them were performed in vitro, which facilitates the non-identification of adverse effects during the reading of the articles.

The cyanogenic substance with the lowest incidence was linamarin being reported by Willie, Collin and Izquierdo (2011). The dose presented by the study was 36 mg and the cyanogenic substance with the highest incidence was tonsil in, where the predominant dose in the articles was 10mg/ml. The extremely high dose of linamarin, which would probably eliminate brain tumors, was very toxic to animals and caused premature death of the same. Thus, it cannot discern whether or not the therapeutic dosage would eliminate the tumor cell.

In the study presented by Garcia-Escudeiro, Gargini and Izquierdo (2008), it reports a positive result regarding the combination of linamarase and linamarin associated with a less toxic level of glucose oxidized. During the study the authors observed that this association increases its therapeutic potential in the cell line of glioblastoma of the dog and its cell death was completed before 48 hours being the IC50 in 48 hours of 50 µg/mL, and when not used glucose oxidized observed that cell death to be completed in 48 hours, ic50 in 48 hours should be 250 µg/mL.

Regarding the action of cyanogenic substances in the tumors present in the articles, we can highlight the study by Mani et al, (2019), which reports that tonsil in acted on prostate cancer cells, inducing a down

regulation of  $\alpha 6$  integrin in DU-145, but not in PC3 cells, which suggests that some exposures of some neoplastic prostate cancer cells may prevent metastatic dissemination.

Makarevic' et al. (2014), observed the effects of tonsil in on the subtypes of integrin  $\alpha$  and  $\beta$ , ILK (integrin-linked kinase) and FAK (focal join kinase), after the treatment of bladder cancer cells (UMUC-3 and RT112) with a dose of tonsil in at 10mg/ml for 24 or 48 hours. To prove the efficacy of tonsil in, the researchers nullify integrin to evaluate the impact of its decline on cell migration and adhering, finding that UMUC-3 and RT112 cell ad take and migration were inhibited after treatment and the expressions of integrin  $\alpha$  and  $\beta$ , ILK and FAK subtypes were all decreased.

In a study conducted with tonsil in therapy, the researchers combined  $\beta$ -glucosity to a tumor associated with a monoclonal antibody (MAb) (HMFG1), this conjugate was tested in vitro for quality and cytotoxicity following tonsil in activation. It was found that only high doses of tonsil in were cytotoxic to HT1376 cells, but exhibited a cytotoxic effect 36 times higher when combined with HMFG1-beta-glucosidase.

According to Liczbiński and Bukowska (2018), they report that in their research they demonstrate the induction by tonsil in apoptosis as an increase in the result of the expression of bax protein and caspase-3 and the reduced expression of ant apoptotic protein BcL-2. Tonsil in has also been widely used in studies to inhibit breast cancer, lung cancer and bladder cancer cells by decreasing integrin expression, which corroborates the stucco of Makarevic et al. (2014).

He et al. (2020), after an analysis in 110 articles on in vivo and in vitro studies on tonsil in, it was suggested that the compound had antitumor, anti-fibrous, anti-inflammatory, immunomodulatory analgesic, anti-atherosclerosis, improving the digestive system, reproductive system, neurodegeneration and myocardial hypertrophy, in addition to reducing glycemia. Furthermore, studies have revealed that tonsil in toxicity is caused by its poisonous product of decomposition of benzaldehyde and hydrogen cyanide after its oral ingestion. When administered intravenously the toxicity was much lower than the oral route.

Regarding the tumors found, lung cancer, nephroblastoma and neuroblastoma, adenocarcinoma, mama cancer, melanoma and Ehrlich tumor are listed. Of the 8 selected studies, 2 were performed in vivo, 2 were performed in vitro, 3 were performed in vivo and in vitro and 1 was performed in humans. According to Saliev et al. (2018), reported in his research that the extremely low frequency magnetic field (50 HZ) could not cause damage to the oxidative base of DNA, but if its intensity is high it can become genotoxic. This corroborates the results obtained in this study, where the frequency of the electromagnetic Field of greatest prevalence was 50 Hz.

Crocetti et al. (2013), investigated that the therapy of the pulsed electromagnetic field of intensity and ultralow frequency can induce apoptosis of human breast adenocarcinoma cells (MCF7). These exposures were cytotoxic to MCF7, but for normal epithelial cells they did not cause any adverse effect. The parameters tested were the frequency of 20 Hz, with intensity of 3mT and duration of 60 minutes/day for up to 3 days. Vadalá et al. (2016), add that a long-term exposure needs to be studied in the concepts that the effectiveness of the pulsed electromagnetic field is linked to signal parameters, duration, exposure magnitude, signal shape, duration of treatment, as well as what will be the cells that will be exposed to the pulsed electromagnetic field.



## Conclusion

It is concluded that cyanogenic substances have been shown to be efficient in reducing tumors, but depending on the dosage given it may be lethal. The magnetic Field has been shown to be efficient in reducing tumors at the frequency of 50 Hz. The main adverse effects produced by cyanogenic substances in the studies were hepatic and renal alterations of electrolytes, cytokines and NF-Kb. In the magnetic Field, the main adverse effects were increased cell damage, reduced apoptosis of tumor cells when the magnetic Field was associated with carboplatin and mild liver injury.

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