Journal of Advances in Medical and Pharmaceutical Sciences

24(8): 1-14, 2022; Article no.JAMPS.86276
ISSN: 2394-1111

Anti-myocardial Infarctus, Efficient Antipoison and Anti-prostate Mighty Spicy Miscellany

A. B. Kunyima [a*], P. D. M. D. Kunyima [a], J. C. Kuburhanwa [a] and M. B. Kunyima [b]

[a] Laboratory of Physical Organic Chemistry, Food and Physical Cardiochemistry, Department of Chemistry and Industry, Faculty of Sciences, University of Kinshasa, P.O.Box-190 Kinshasa XI, Democratic Republic of Congo.
[b] High School of Medical Technics Hospital, Kinshasa/N'djili, Democratic Republic of Congo.

Authors' contributions

This work was carried out in collaboration among all authors. Author ABK designed and supervised the study, wrote the protocol and wrote the draft of the manuscript. Author PDMDK is the experimentalist of the results of this paper. Authors JCK and MBK managed the proof reading and correction of manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2022/v24i8569

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/86276

Original Research Article

Received 02 March 2022
Accepted 07 May 2022
Published 20 September 2022

ABSTRACT

Background: Cardiovascular diseases, cancers and diabetes that are the main cause of mortality in the world have as principal origine the lack of food (life) hygiene and environmental pollution at which it should be added the synthesis chemical products and the poisons playing a prominent and active role in this human drama. In this paper it is shown that with spicy blend rationally performed on the basis of their natural properties, prostate and myocardial infarction can be healed. Also this mixture can treat some poisons when detected before.
Aim and Objective: The laboratory of physical organic chemistry, food and physical cardiochemistry, Lacopa-CCP in acronym, has just developed a powerful blend of spices based on Turmeric called PdeluxeKK (Paulin Deluxe KUNYIMA KUNYIMA), conceived at the beginning to treat a myocardial infarction caused by poisoning clinically established and after become unexpectedly efficient in the treatment of a prostate and other poisons.
Methodology: This mixture contains in order turmeric in large quantity, ginger, black pepper, garlic and red onion, original pure honey and the variant of PdeluxeKK incorporates at the end before the honey the red beetroot to make this mixture more reliable against cyanide poisons through its

**Corresponding author: E-mail: anaclet.kunyima@unikin.ac.cd;*

betacyanin and to prevent eventual anemic problems during the treatment. The order of the mixture is of great importance because it has been observed that its effectiveness changes not only with the proportions of the components involved but also according to the order of addition of the components which constitute this mixture. The mixture pastry should be kept between - 5°C and 0°C.
Results: Prostate and myocardial infarction clinically established have been satisfactorily treated by PdeluxeKK. Also many poisons detected in human body are successfully treated by PdeluxeKK.
Conclusion: This mighty spicy miscellany successfully treats prostate, myocardial infarction and certain poisons.

Keywords: Black pepper; garlic; ginger; honey; PdeluxeKK; red beetroot; red onion; turmeric.

1. INTRODUCTION

The lifestyle of modern man, following the search for well-being, exposes him to several diseases due to the variation in the balance of man and nature as well as to the modification of his food, especially today based on the genetically modified organisms (GMOs).

We speak today of the excessive pollution of the air caused by the adventures of man, in search of material goods. According to a March 2014 WHO study, 7 million of people worldwide died prematurely from the effects of air pollution[i].

The scientific community is now unanimous in confirming that air pollution has significant impacts on our health, both in developed and developing countries, and that it is not the prerogative of large cities, with rural areas also showing high levels of pollutants.

During episodes of acute air pollution and the few days that follow, there is an increase in the rates of hospitalization, mortality, heart attacks and pulmonary disorders, an aggravation of existing chronic diseases, heart (arrhythmia, angina, infarction, cardiac insufficiency) or respiratory (chronic obstructive pulmonary disease, respiratory infection, asthma attack). The appearance of eye irritation and inflammation of the mucous membranes of the respiratory tract.

Long exposure to this pollution can contribute to the onset and aggravation of many conditions such as cardiovascular diseases, myocardial infarction, strokes, angina pectoris, lung diseases such as asthma and chronic bronchitis, many cancers, particularly of the lungs and bladder, impaired development of the lungs of children.

As a preventive and curative measure for all the health problems mentioned above, Lacopa-ccp has developed a PdeluxeKK potion to help extend the life expectancy of modern man.

2. MATERIALS AND METHODS

2.1 Materials

The turmeric rhizomes and the rhizomes of ginger, black pepper, garlic, red onion, original pure honey, red beetroot are purchased on the Kinshasa market. After being cleaned with water and dried, the spices are brought to the mill to be ground.

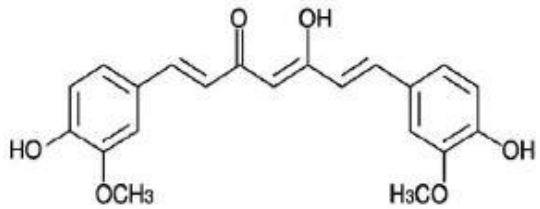
1) *Curcuma longa* L.

The main active ingredient of turmeric, curcumin, along with curcuminoids, does indeed have anticancer activity [1], although we do not yet know all the mechanisms and make this spice a powerful antioxidant[i]. It is an ancestral remedy against gastric acidity and other digestive disorders, as it stimulates the secretion of mucus and thus protects the stomach. It also alleviates nausea [2]. It is completely indicated in the digestive disorders related to the laziness of the liver. It has traditionally been used as a choleretic or cholagogue, also used in the symptomatic treatment of functional digestive disorders attributed to a hepatic origin and finally used as an appetite stimulant[ii]. It is an anti-inflammatory (asthma and eczema) [2]. Turmeric has a cholesterol-lowering effect and intervenes in the prevention of cardiovascular risks [2]. Applied to the skin, turmeric treats several types of conditions including psoriasis and fungal infections [2]. The medicinal properties of curcumin, this miracle compound, are very numerous [3]. Curcumin acts on multiple targets and thus influences many molecular and biochemical cascades. These molecular targets include transcription factors, growth factors and their receptors, cytokines, enzymes, genes regulating cell proliferation and apoptosis.

Curcumin interacts with many targets. It binds to growth factor receptors, metals, albumin and other molecules and inhibits the activity of enzymes [4-26].

2) Ginger

Ginger rhizomes are rich in carbohydrates, lipids and proteins. They contain iron, calcium, magnesium, manganese, sodium and phosphorus. Ginger contains vitamin B, vitamin C which disappears once the ginger is dried. Its active ingredient is gingerol ($C_{17}H_{27}$ O_4), a phenolic compound from the vanilloid family which has an anti-inflammatory, antioxidant and antiemetic action. It acts against certain cancers. Associated to other spices, ginger is a very powerful antibacterial and antiviral that can be used in case of cough, flu or cold. It also relieves throats soreness and warms. It is an excellent stimulant for the immune system which becomes more resistant. It relieves muscle and joint pain in the event of fractures, sprains, tendonitis or rheumatic diseases. It protects the digestive system and facilitates intestinal transit.



1,7-bis (4-hydroxy-3-méthoxy-phényl) hepta-1,6-diène-3,5-dione

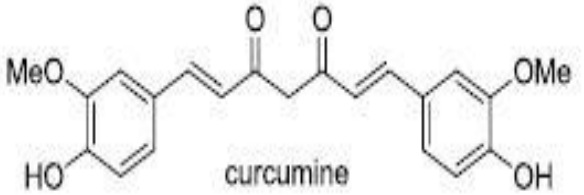
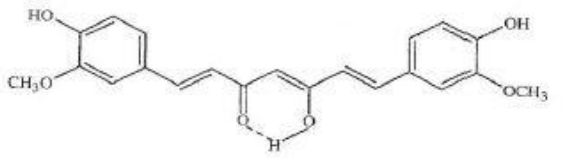
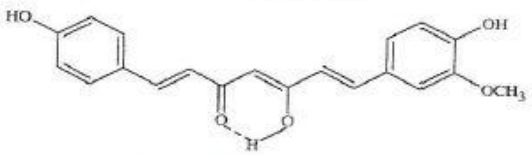


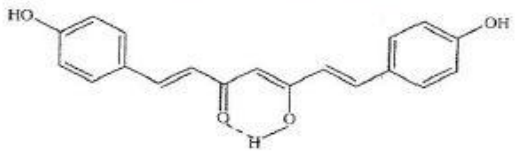
Fig. 1. Chemical structure of curcumin



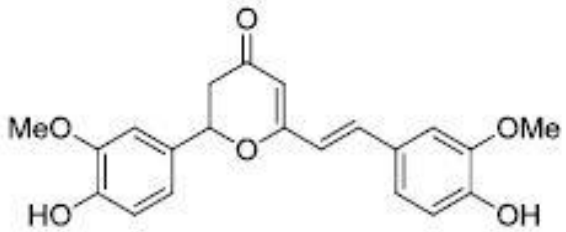
Curcumin



Demethoxycurcumin



Bis-demethoxycurcumin



Cyclocurcumin

Fig. 2. Chemical structure of curcuminoïds

It is an excellent appetizer, relieves vomiting. It reduces the level of bad cholesterol. It is an excellent energizer and a good aphrodisiac. Its antibacterial properties are enhanced when consumed with turmeric or garlic [27].

3) Garlic

Its main active principle is allicin, which is an organosulphur compound abundant in garlic in a somewhat more complex form, as it is also found in onions, porous and in other species of the family of liliaceae and alliaceae. Allicin is a colorless liquid with a characteristic pungent odor. It has anti-bacterial and antifungal properties [28,29]. It has a thiosulfate functional group, R-S (=O)-S-R. This compound is not present in garlic as far as it does not undergo tissues damages [30].

If this happens, allicin is formed by the action of the enzyme alliinase on alliin [30].

Allicin is chiral (the sulfur atom bearing the oxo is asymmetric) and only the S enantiomer appears naturally. The racemic mixture can be formed by oxidation of allyl disulfide [31].

$(SCH_2CH=CH_2)_2+RCO_3H \rightarrow CH_2=CHCH_2S(O)SCH_2\,CH = CH_2 + RCO_2H$

with RCO_3H = meta-chloroperbenzoic acid.

The enzyme alliinase is irreversibly deactivated by a pH < 3. Thus, allicin is generally not produced in the body of a consumer of fresh or powdered garlic [32,33].

In addition, allicin is unstable, degrading in 16 hours at 26°C [34].

Allicin can: reduce arteriosclerosis and fatty deposits in the arteries [35,36], normalize lipoprotein balance and reduce blood pressure [37,38], have anti-thrombosis properties [39], anti- inflammatory and antioxidant of some importance [40,41,42]. Other studies have shown a strong oxidative effect in the intestine that is harmful to intestinal cells [43]. Allicin works by scavenging harmful free radicals. They are the sulfenic acids (acid-2-propenesulfenic) produced by the decomposition of allicin which react extremely quickly with free radicals by binding to them. Allicin has anti-bacterial activity [44,45].

4) Black pepper

The main component of black pepper is piperine (or 1-piperoylpiperidine), a pungent alkaloid. On the Scoville scale, piperine is less pungent (100,000 SHU = Scoville heat unit) than capsaicin (16,000,000 SHU), one of the pungent components of peppers, but more than 6-gingerol, the pungent compound of ginger (60,000 SHU) [46,47,48].

Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is a chemical compound of the family of alkaloids, active compound of red pepper. Piperine (Tfusion = 130°C, poorly soluble in water, soluble in alcohol, chloroform, ether, isopropanol, density = 1.193 g/cm3) has antimicrobial, anti-inflammatory and hepatoprotective properties.

It promotes the absorption as well as the bioavailability of many molecules (vitamins, minerals, drugs, polyphenols, etc.) in the body. Some molecules, such as curcumin, see their bioavailability multiplied by 20 when combined with piperine thanks to a decrease in hepatic clearance [49,50].

5) Beetroot

Its red color makes it the ally of blood cells, thanks to the iron it contains and which allows the regeneration of blood. It therefore promotes the supply of oxygen in the body, thus improving blood circulation by dissolving inorganic calcium deposits.

In addition to a concentrate of vitamins, vitamins A, B_1, B_2, B_4, B_5, B_6, B_9 (folic acid against fatigue, loss of appetite and anemia), C, B, K, PP, beetroot has calcium, potassium, iron, magnesium, zinc, selenium, copper, manganese, sodium, phosphorus as well as beta-carotene and betacyanin ($C_{24}H_{27}N_2O_{13}$), a glucose heteroside (5-o-glucose betanidine) which is an extremely soluble pigment giving the Red color. This pigment is found in the vacuoles of all plants and in animal cells. Red beetroot has 90% of sucrose and the rest is divided into pentosans, hexosans, glucose and fructose; it also contains fibers. Beetroot is regenerating, anti-hypertension, detoxifying, anti-cancer, anti-cholesterol, and anti-stress. It eliminates toxins, heavy metal salts and radionuclides from the body, strengthens the walls of blood vessels and improves the functioning of the digestive system. It has a strong laxative effect, it is used for weight loss. It helps to deal with menstrual irregularities, menopause and increases the sexual activity of men [iii].

It cleans the liver and thus allows it to store sugar, thus contributing to the reduction of sugar in the blood. Raw red beetroot, which has a moderate glycemic index of 30 in the green zone, exhibits a low glycemic charge that means its ability to elevate blood sugar levels based on a common serving is low and therefore it is recommended for people with diabetes, especially when eaten raw [iv].

6) Red onion

Allicin is found in onions in general. The onion is a source of vitamins (PP, H, E, B1, B_2, B_5, B_6, B_9), calcium, zinc; fluorine, iron, cobalt, phosphorus, nickel, aluminum, chromium, boron, manganese, copper, iodine, potassium, sodium, selenium and even essential oils [51-56].

It contains organic acids, proteins, starch, monosaccharides, disaccharides, it is not too rich in calories. It stimulates the appetite, improves digestion, it is antiseptic and antibacterial. It fights hypotension and prevents the development of cancer cells.

It fights viruses, promotes the assimilation of food and increases the body's resistance to many infections. This vegetable is widely used in disorders of the gastrointestinal tract. It helps to cope with atherosclerosis, general weakness in colds, and decrease of sexual activity. In medicine, it is used to combat scurvy and is widely used as an anthelmintic. Fresh juice of this vegetable with honey is able to cure bronchitis, cough and even fungal skin disease.

This ingredient is recommended for use in dermatitis, for the removal of warts and calluses. Its high content of quercetin (flavonoid) makes it play the role of a powerful antioxidant involved in the prevention of liver fibrosis. It has a beneficial action on the cardiovascular system. It inhibits platelet aggregation (when fresh), hence a lower risk of clot formation. It exerts a hypoglycemic action by its sulfur compounds and the diphenylamine of which it is rich. Quercetin protects against LDL oxidation. The onion, which also has fibers, opposes microbial proliferation, and thus plays an anti-bacterial role, especially against gram + bacteria. It will keep for up to two months in a dry, cool and dark place. Red onion helps to prevent osteoporosis, thanks to its high content of quercetin, an antioxidant from the family of polyphenols whose activity is higher than that of isoflavins. In addition, the onion contains silica, which is good for the arteries and facilitates the fixation of calcium in the bones. The onion has a diuretic action which is due, it seems, to the presence of fructosans, these particular carbohydrates, abundant in the bulb, and probably to the high potassium / sodium ratio. This results in the effectiveness demonstrated by the urinary system and on the prostate with better transit and a limitation of infections. Onion opposes an excessive rise in blood sugar levels. The active principles are certain sulfur constituents (allyl and propyl disulphide) and a specific amine (diphenylamine). The high consumption of onion allows the removal of dropsy. The onion limits the infiltration of serous fluid in the organs which may cause edema. It should be noted that the selenium contained in the onion is an antioxidant fighting against aging, it is an anticancer.

7) Honey [57,58]

The color and composition of honey depends on its origin and the materials used by the bees for its production. The benefits of honey are multiple and different depending on the type of honey. Honey contains fewer calories than sugar (64 calories against 84 for 20 g). It has the same glycemic index, but provides more antioxidants. Honey contains carbohydrates in large quantities (78 to 80%) including 38% fructose (or levulose) and 31% glucose (or dextrose) as well as maltose, sucrose and various other polysaccharides. It contains 17% water, proteins (less than 1%, but containing a very large number of free amino acids such as aspartic acid, glutamic acid, alanine, arginine, asparagine, cystine, glycine, histidine, isoleucine, leucine , lysine, methionine, phenylalanine, proline, serine, tryptophan, tyrosine and valine); mineral salts (0.3% for nectar honey, up to 1% for honeydew honey, with more than thirty elements already inventoried such as aluminum, silver, arsenic, barium, beryllium, bromine , calcium, cesium, chlorine, chromium, cobalt, copper, iron, lithium, magnesium, manganese, mercury, molybdenum, nickel, gold, palladium, phosphorus, potassium, rubidium, scandium, silicon, sodium, sulfur, strontium, titanium, vanadium , zinc, zirconium); these mineral elements are not always all present in a specific honey. Some of them are systematically present in all honeys and often then in large quantities, in particular potassium, the first intracellular cation essential to life. Dark honeys are overall quantitatively richer in mineral matter than light honeys. Honey contains organic acids (free or combined in the form of lactones (0.3%), the

main one being gluconic acid); a large number of vitamins (mainly vitamins B_1, B_2, B_3 (or vitamin PP), B_5, B_6, C and incidentally vitamins A, B_8 (or vitamin H), B_9, D, K).

It contains lipids in tiny amount, in several forms (triglycerides, fatty acids such as palmitic acid, oleic acid and linoleic acid). Many organic compounds are found there:

- Enzymes, the main ones being alpha and beta amylases, gluco-invertase and gluco-oxidase; these enzymes (which facilitate the digestion of food and are at the origin of certain virtues of honey) are destroyed by excessive heating of honey, which should therefore always be avoided.
- Several natural antibiotic factors, grouped under the generic name of inhibin, which are in fact powerful bacteriostatics, that is to say that they prevent the development of bacteria but do not kill them.
- Many other various biological substances:

1. A cholinergic principle close to acetylcholine,
2. An estrogen principle,
3. Flavonoids endowed with multiple and interesting physiological properties,
4. Alcohols and esters,
5. Aromatic substances which not only give the aroma (like phenylacetic acid) and the specific taste of a given honey, but which also have therapeutic virtues;
6. Pigmentary materials, specific to each honey, which give it its own color.

And finally, we find pollen grains in honey that signify its botanical origin. A source of longevity, honey slows down the physiological processes of aging and reduces the premature weakening of vital functions. Rich in carbohydrates (3/4 of its weight), honey provides energy and is digested well, much better than sugar. Low in sucrose, its assimilation does not produce any toxins in the body. It activates the healing of burns and wounds when applied externally, and reduces throat irritation. It is an ideal food for children, students, convalescents and athletes. It solves the problems of hypertension and hypotension, heart problems, arthritis, colds, constipation, dyspepsia, acidity and insomnia. It provides decongestion of the bronchi and lungs, treats oral problems; can be used in cosmetics thanks to its calming and anti-inflammatory properties; in inflammation of hemorrhoids (external use), being an alkaline food it does not usually cause problems of assimilation in people with poor digestive functioning, being of great help in the healing of ulcers stomach and duodenum. Its richness in potassium transforms it into a bactericide, preventing the development of cultured microorganisms, which is why it has been used since antiquity as a food preservative. It acts as an effective disinfectant and wound healer. Honey improves vitality, provides a solid and clear stimulation of physical activity (overall improvement in performance), an increase in resistance to stress, fatigue, cold, infections (strengthening of natural defences). Honey contributes to the slowing down of physiological aging, and a probable improvement in sexual activity. It ensures greater psychic activity: stimulation of mood, strengthening of the will, desire and pleasure in working, reduction of emotionality and better intellectual activity (improvement of memory). It contributes to the regulation and overall regeneration of major organic functions; everything is done without disturbing the natural rhythm of the body.

2.2 Methods

Garlic and red onion are both ground and exposed to air during at least 15 minutes before joining mixture of turmeric-ginger-black pepper-garlic+onion-red beetroot-honey. In this mixture turmeric is in large quantity.

Mixing is done in this order:

Turmeric + ginger + black pepper + (garlic and red onion) + original pure honey and PdeluxeKK's variant in this order: turmeric + ginger + black pepper + (garlic and red onion) + red beetroots + original pure honey. The whole pastry is thus preserved in honey and put in the fridge between -5°C and 0°C. Avoid light which would cause photo degradation, avoid buffered basic aqueous media, cell culture medium, and human plasma to avoid chemical degradation.

Avoid reactive oxygen species such as: 0H, 0_2^-, R00$^\cdot$, N0$^\cdot$, radical glutathione GS$^\cdot$, H_20_2, $^1 0_2$ to combat the degradation or structural modification of curcumin i.e. intramolecular cyclizations or induced polymerization [59,60].

The quantities involved in this PdeluxeKK mixture remain the property of the laboratory until a patent is obtained, likewise the posology.

Fig. 3. The variant of PdeluxeKK

3. RESULTS AND DISCUSSION

The laboratory of physical organic chemistry, Food and physical cardiochemistry of the Faculty of Sciences, University of Kinshasa/DRC has just developed a turmeric-based mixture that treats the prostate and myocardial infarction in record time. This mixture called PdeluxeKK has successfully treated poisoned patients. Tests carried out on these patients revealed poisoning, but the nature of the poison cannot be said at this time. Based on the structure of the curcuminoïds present in turmeric, this mixture could cure cyanide poisons, nuclear poisons, chemical poisons of all kinds, biological poisons (viruses, bacteria). It is composed of turmeric + ginger + black pepper + (garlic + red onion) + pure honey in this well-defined order and in well-defined proportions and well-kept cool (between -5°C and 0°C).

A person whose PSA was equal to 14.5 in 2020 was followed for 4 months and the decrease of his PSA at 4 has been observed.

A person whose myocardial infarction has been clinically established is completely cured after treatment with PdeluxeKK during 3 months.

These two cases were so striking and so amazing that the laboratory decided to quickly publish them as very important scientific information, experiments are continuing.

Several people (43 persons) were completely cured after an established poisoning and this within a week.

The nature of the poisoning has not been established as it is known that there are several poisons such as chemical poisons, biological poisons and nuclear poisons. Lacopa-ccp is continuing to research this.

It has been observed that when you change the order of the mixture, you change its efficiency. This mixture has been found to be a potent anti-poison and could be used in cancer studies.

Information on the physico-chemical properties of curcumin, an essential component of turmeric, is important for the eventual interpretation and understanding of the results.

Indeed, curcumin is a complex compound made up of chemical functions that can change depending on the direct environment, the presence of different types of solvents, temperature and the presence of light. It is an unstable and heat-sensitive product.

It is an amphiphilic compound because it has a center and polar ends which are separated by two apolar unsaturated links. Curcumin can exhibit interactions due to its hydrogen bond donor and acceptor capacities coming from the central β-dicarbonyl link, then those that can take place with the hydroxy groups present on the phenyl nuclei of the ends. There are also hydrogen bonds that can take place via the oxygen of the ether functions on the methoxy groups. Then there are the chelating properties of multivalent metallic and non-metallic cations, its fairly high partition coefficient, the activities

made possible thanks to the free rotations around the multiple C-C bonds and finally the biological effects allowed by its ability to react like a Michael acceptor, i.e. the chemical reactivity capacity of curcumin to promote covalent-type interactions with targets possessing nucleophilic functions such as thiols, thiolates or amines. It has been established that Michael acceptor molecules are inducers of protective enzymes of carcinogenesis and that their activity occurs with thiol or thiolate functions. These molecules include chalcones, cinnamates, coumarins, bis (benzylidene)-acetones and curcuminoids [61].

The most illustrative example is that of reduced glutathione (GSH). This tripeptide of the sequence glutamate-cysteine-glycine has a thiol function making this peptide a Michael donor. Incubation of curcumin with a concentration gradient of GSH leads to a proportional and time-dependent decrease in the absorbance at λ=430 nm of curcumin in protic solvents which means that electronic delocalization is interrupted on the central part of curcumin because it reacts with GSH. The formation of these adducts also indicates that curcumin interferes with the redox metabolism of cellular glutathione.

This covalent mechanism can also intervene with seleno-cysteine residues of seleno-proteins.

The irreversible inhibitory activity of curcumin has been demonstrated by its covalent attachment to thioredoxin reductases. These cystosolic, mitochondrial and nuclear enzymes constitute a system, analogous to the glutathione-glutathione reduced system, capable of trapping free radicals [62]. Curcumin binds to it via selenium and sulfur residues and prevents them from exerting their reducing power, an activity sought in oncology in order to promote cellular apoptosis induced by the toxicity of free radicals. These properties to react with Michael donors play an important role in the ability of curcumin to covalently and therefore irreversibly disrupt the binding sites of certain enzymes to their substrates. This contributes to the pleiotropic action of this natural compound.

As for the hydrogen bond donor and acceptor capacities, it must be said that the behavior of the β-diketone nucleus of curcumin differs from the typical behavior of classic β-diketones such as acetylacetone with respect to the keto-enol balance.

In general, these molecules are in diketone form in solvents with high relative permittivity (ε_r) or polarity, such as water or dimethylsulfoxide, and in enol form in solutions with low permittivity, such as cyclohexane or dichloromethane. The β-diketone of curcumin actually exists preferentially in the enol form both in protic polar solvents such as water and in cyclohexane.

This tendency for the equilibrium to shift to the enol form has been confirmed by Fourier transform I.R [63,64].

This assertion has however been balanced by Balasubramanian in 2006 showing by orbital study that in apolar solvents, the enol and keto forms are co-dominant [63,65].

The direct chemical environment in which curcumin is located therefore determines the different conformations of this β-diketone part of the molecule and will therefore condition its ways of interacting with other compounds. In apolar solvents, curcumin is in the form of a cis-enol tautomer formed in which the proton is considered symmetric in a delocalized electron system. In these solvents, the enol proton and carbonyl oxygen do not allow hydrogen bonds.

Conversely, in polar solvents this delocalized intramolecular system is disturbed and, with increasing permittivity, the equilibrium tends to shift towards an open enolic tautomer which allows the creation of strong hydrogen bonds.

Therefore, in a physiological situation, this open enol tautomer interacts with water in plasma and cytosol, or with polar amino acids present on target or transport proteins directly or through water molecules. To summarize, the study of hydrogen interactions mediated by the β-diketone function of curcumin allows us to determine the way in which it interacts with the proteins on which it has an activity.

Among these we can cite tubulin [66] and glycogen synthase kinase – 3 β or GSK-3β which is involved in disturbances of the phosphorylation of the Tau protein in neurodegenerative pathologies such as Alzheimer's [67].

Tubulin is an essential component of the microtubules of the cellular cytoskeleton and plays a major role, through polymerization/depolymerization processes, in the transport of duplicated chromosomes during mitotic anaphase. This property is interesting and has been extensively studied in the field of oncology.

Indeed, one of the main characteristics of a cancer cell is to multiply rapidly. Curcumin, by binding to tubulin to prevent its polymerization, no longer allows microtubules to perform their functions as chromosomal transporters for the distribution of genetic material in each daughter cell and leads to blockage of the cell cycle. Curcumin is therefore said to be anti-cancer, anti-proliferative and one of the actions attributed to it is this action on the mitotic spindle.

In the same way as the central β-diketone function, the hydroxyl groups present in the para position at the ends of curcumin have a strong capacity for interaction with several protein targets or transporters. These additional abilities multiply the binding capacities and explain the pleiotropic behavior of curcumin.

The amino acids carried by proteins of therapeutic interest interacting with curcumin are Gln 11 and Lys 254 (porcine tubulin); Asp 1 Ser 26 and Lys 28 (Beta-amyloid peptide); Val 135, Arg 141 and Lys 85 (GSK-3β) [63].

In particular, the hydrogen bond donor sites of curcumin with lysine 28 and phenylalanine present on the hexameric β-amyloid peptide can be identified. These binding points with curcumin are of interest in the context of research on neuroprotective activities [68].

The oxygen atom involved in this ether function of curcumin is the only one that can only accept a hydrogen bond. To date, interactions mediated solely by these methoxy groups have not been described, but they contribute to promoting interactions such as with Lys 28 present on the βA peptide.

This keto-enol balance leads to changes in the physical characters of curcumin in terms of its light absorption spectrum. Curcumin is a compound which has an absorption wavelength λmax in the visible range which varies according to its form, diketone or enol, and the nature of the solvent in which it is dissolved.

This spectral modulation is very important and intervenes in the field of biological evaluations, including those of curcumin. In water where the enolic form predominates, its λ max = 430 nm; λ max = 435 nm in dimethyl sulfoxide (DMSO) in the enol form whereas its diketone form admits λ max = 454 nm.

As if to enhance the power of hydrogen bond donor and acceptor sites, curcumin is able to spatially conform to a constraint given by a molecular target. There are also different configurations that it can adopt thanks to the double bonds which are 3 in number in the enolic form. Thus, the central liker can be likened to an articulated arm that promotes as many interactions as possible between curcumin and its targets. In polar solvents or in cells, curcumin is in the open enol tautomeric form and “cis-to-trans” isomerizations can then take place around the alpha carbon of the enol [64]. Overall, curcumin is able to bind to many biological molecules thanks to its structural adaptation which is exploited in order to maximize the number of intermolecular bonds with its targets. This ability once again explains the pleiotropic nature of its natural properties.

As for the chelating properties of multivalent metallic and non-metallic cations, the central β-diketone part of curcumin acts like all β-diketones with regard to the chelati.

It binds to boron, copper, aluminum, magnesium, zinc, lead, cadmium, ferric iron, ferrous iron and selenium. Most scientific sources indicate that the metal cations are bound by the oxygen of the diketone form, but some also propose chelation sites on the non-binding doublets of the oxygens of the methoxy groups [69]. This chelation capacity is very interesting because it is also the way for curcumin to bind indirectly to proteins using metal atoms or metalloproteins.

Insofar as half of the proteins contain metals and knowing that approximately 1⁄3 need metals to function correctly, this property of binding to metalloproteins constitutes a chemically important phenomenon with biological repercussions that can be exploited in various chemical fields.

Through this discussion it is recalled the pleiotropic capacities of curcumin that explain its large therapetic potential when it is alone. When it is blended with the other wonderful chemical compounds, its healing power is emphasized, specially when those compounds have also healing properties. It is noteworthy to see that all those compounds added to curcuma have all kind of vitamins, mineral elements and certains organic compounds. This beyond the therapeutic potential of curcumine there is conjugation of effects and their increase with the conjunction of other spices. For example the black pepper added to curcuma increases its bioavailability, that means the curcumin assimilation in the

organism [70]. Association of ginger to curcummin enhances the anti-inflammatory effects of curcumin [70]. Addition of red beetroot at the mixture allow to treat cyanide poisons by means of its betacyanin during the treatment and to prevent anemic state that can occur during the treatment [ix]. Honey, besides its wonderful natural properties, has been used as pastry preservative. Things are the same for the other components of this mixture. Nowadays a lot of researches on turmeric or on turmeric mixture with the other compounds are performed through world laboratories where curcuminoids behavior is diversely commented [71,72,73].

4. CONCLUSION

In addition to treating prostate, myocardial infarction, PdeluxeKK (Paulin de Luxe KUNYIMA KUNYIMA) is an effective mixture against cyanide poisons, against poisons of some metals such as mercury (Hg), lead (Pb), Selenium (Se), Aluminum (Al), Boron (B), Cadmium (Cd).

It can be used against certain cancers. Poisoned patients testify that the mixture makes insomnia disappear.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Aggarwal BB, Shishodia S, Takada Y, Et AL. Curcumin suppresses the paclitaxel-induced nuclear factor-kappaB pathway in breast cancer cells and inhibits lung metastasis of human breast cancer in nude mice. Clin Cancer Res. 2005;11:7490-8.
2. La Rousse. Encyclopédie des plantes médicinales. Identification, préparations, soins. Paris: Larousse/VUEF 2001:92
3. Dikshit M., Rastogi L., Shukla R., and Srimal R. C. Prevention of ischaemia-induced biochemical changes by curcumin & quinidine in the cat heart. Indian J Med Res. 1995;101:31 – 35.
4. Zsila F, Bikadi Z, Simonyi M. Circular dichronism spectroscopic studies reveal pH dependant binding of curcumin in the minor groove of naturel and synthetic nucleic acids. Org Biomol chem 2004, 2: 2902 – 10.
5. Takeuchi T, Ishidoh T, Iijima H, Et AL. Structural relationship of curcumin derivatives binding to the BRCT domain of human DNA polymerase lambda. Genes cells. 2006;11:223 – 35.
6. Kunwar A, Barik A, Pandey R, Priyadarsini KI. Transport of liposomal and albumin loaded curcumin to living cells: An absorption and fluorescence spectroscopic study. Biochem Biophys Acta 2006, 1760:1513 -20
7. Pulla Reddy AC, Sudharshan E, Appu Rao AG, Lokesh BR. Interaction of curcumin with human serum albumin – a spectrosccopic study. Lipids. 1999;34:1025 – 9.
8. Zsila F, Bikadi Z, Simonyi M. Induced Circular dichroism spectra reveal binding of the anti – inflammatory curcumin to human alpha 1 – acid glycoprotein. Bioorg. Med Chem. 2004;12:3239 – 45
9. Bilmen JG, Khan SZ, Javed MH, Michelangeli F. Inhibtion of serca Ca2+ pumps by curcumin. Curcumin putatively stabilizes the interaction between the nucleotide – binding and phosphorylation domains in the absence of ATP. Eur J Biochem. 2001;268:6318 – 27.
10. Reddy S, Aggarwal BB. Curcumin is a non – competitive and selective inhibitor of phosphorylase kinase. FEBS Lett. 1994;341:19-22
11. Shim JS, Kim JH, Cho NY, Yum YN, Kim SH, Park HJ, Et AL. Irreversible inhibition of CD 13/aminopeptidase N by the antiangiogenic agent curcumin. Chem. Biol. 2003;10:695 – 704.
12. Aggarwal BB, Bhatt ID, Ichikawa N, Ahn KS, Sethi G, Sandur SK, Et AL. Curcumin – biological and medicinal properties. Tumeric: the genus curcuma. Taylor and Francis Group. 2006;297 -368.
13. Awasthi S, Pandya U, Singhal SS, Et AL. Curcumin – glutathione interactions and the role of human glutathione – s – transferase P1-1 Chem Biol Interact. 2000;128:19–38.
14. Benkoussa M, Celine Brand C., Demottem H. Et AL. Retinoic Acid Receptors Inhibit AP 1 Activation by Regulating Extracellular Signal-Regulated

Kinase and CBP Recruitment to an AP1-Responsive Promoter. Mol Cell Biol. 2002;22(13):4522-4534.

15. Bharti AC, Donaton, Singh S, Aggarwal BB. Curcumin(diferuloylmethane) down-regulates the constitutive activation of nuclear factor- kappa B and IkappaBalpha kinase in human multiple myeloma cells, kading to suppression of proliferation and induction of apoptosis. Blood. 2003;101(3):1053 – 62.
16. Iersel ML, Ploemen JP, Struik I, Van Amersfoott C, Et AL. Inhibition of glutathione-s tranferase activity in human melanoma cells by alpha, beta-unsaturated carbonyl derivatives. Effects of acrolein, cinnamaldehyde, citral, crotonaldehyde, curcumin, thacrynic acid, and trans-2-hexenal. Chem Biol Interact. 1996;102:117-32.
17. Jung Y, Xu W, Kim H, Ha N, Neckers L. Curcumin-induced degradation of Erb B2: A role for the E3 ubiquitine ligase CHIP and the Michael reaction acceptor activity of curcumin. Biochim Biophys Acta. 2007;1773:383-90
18. Leu TH, Su SL, Chuang YC, Maa MC. Direct inhibitory effect of curcumin on src and focal adhesion kinase activity. Biochem Pharmacol. 2003;66:2323-31.
19. Skrzypczak – Jankun E, Zhou K, Mccabe NP, Selman SH, Jankun J. Int J Mol Med. 2003;12:17-24.
20. Gupta KK, Bharne SS, Rathinasamy K, Naik NR, Panda D. Dietary antioxidant curcumin inhibits microtubule assembly through tubulin binding. FEBS J 2006, 273: 5320-32.
21. Wortelboek HM, Usta M, Van Der Velde AE, Et AL. Interplay between MRP inhibition and metabolism of MRP inhibitors: the case of curcumin. Chem Res toxicol. 2003;16:1642-51.
22. Kunwar A, Barik A, Pandey R, Priyadarsini KI. Transport of liposomal and albumin loaded curcumin to living cells: An absorption and fluorescence spectroscopic study. Biochim Biophys Acta. 2006;1760:1513 -20.
23. Yang F, Lim GP, Begum AN, Et AL. Curcumin inhibits formation of amyloid beta oligomers and fibrils, binds plaques, and reduce amyloid *In vivo*. J Biol Chem. 2005;280:5892-901.
24. Fang J, Lu J, Holmgren A. Thioredoxin reductase is irreversibly modified by curcumin: A novel molecular mechanism for its anticancer activity. J Biol Chem. 2005;280:25284-90.
25. Martin-Cordero C, Lopez- Lazaro M, Galvez M, Ayuso MJ. Curcumin a DNA to poisomerase II poison. J Enzyme Inhib Med Chem. 2003;18:505-9.
26. Mullally JE, Fitzpatrick FA. Pharmacophore model for novel inhibitors of ubiquitin isopeptidases that induce p53-independent cell death. Mol Pharmacol. 2002;62:351-8.
27. Julien Eymard: Gingembre, Sainte santé, Traitements, Phytothérapie, Plantes médicinales 2016, 27 avril
28. Allicin, the Antibacterial Principle of Allium sativum. I. Isolation, Physical Properties and Antibacterial Action, Chester J. Cavallito; John Hays Bailey; Journal of the American Chemical Society. 1944;66:1950-1951.
DOI: 10.1021/ja 01239a048
29. Stephen R. Davis, “An overview of the antifungal properties of allicin and its breakdown products- the possibility of a safe and effective antifungal prophylactics”, Mycoses. 2005;48:95-100 (ISSN 0933-7407).
PMID 15743425
DOI 10.1111/j.1439-0507.2004.01076.x)
30. (en) Eric Block, “ The chemistry of garlic and onions”, scientific American, 1985;252(3):114-119
31. Flavor components of garlic extract, Brodnitz, M.H.; Pascale, J.V.; Derslice, L.V.; J.Agr. Food.chem. 1971;19(2):273-275.
32. An introduction to Organosulfur chemistry, R.J. Cremlyn, John Wiley and Sons: Chichester (1996). (ISBN 0471955124).
33. Stability of allicin in garlic juice, Yu. TH, Wu, CM. J. Food Sci. 1989;54(4):977-981.
34. (en) G hahn (éd. HP Koch et LD Lawson), Garlic: the science and therapeutic application of Allium sativum L and related species (2nd edn), Baltimore, Williams and wilkins.1996;1-24.
35. (en) S.Eilat, Y. Oestraicher, A. Rabinkov, D. Ohad, D. Mirelman, A. Battler, M. Eldor et Z. Vered, “Alteration of lipid profile in hyperlipidemic rabbits by allicin, an active constituent of garlic”, Coron. Artery Dis., 1995;6:985-990
36. (en) D. Abramovitz, S. Gavri, D. Harots, H. Levkovitz, D. Mirelman, T. Miron, S. Eilat-Adar, A. Rabinkov, M. Meir Wilchek, M. Eldar and Z. Vered, “Allicin-induced decrease in formation of fatty streaks

(atherosclerosis) in mice fed a cholesterol-rich diet", Coron. Artery Dis., 1999, 10 :515-519.
DOI: 10.1097/00019501-199910000-00012

37. (en) CA Silagy et HA Neil, "A meta-analysis of the effect of garlic on blood pressure", J Hyportens. 1994;12(4):463-468
38. (en) A. Elkayam, D. Mirelman, E. Peley, M. Meir Wilchek, T. Miron, A. Rabinkov, M. Oran-Herman et T. Rosenthal, "The effects of allicin on weight in fructose-induced hyperinsuline mic, hyperlipidemic, hypertensive rats. Am. J. Hypertens. 2003;16:1053-1056.
DOI: 10.1016/j.amjhyper.2003.07.011
39. (en) Srivastava KC, "Evidence for the mechanism by which garlic inhibits platelet aggregation." Prostaglandins Lenkot Med. 1986;22(3):313-321.
DOI: 10.1016/0262-1746(86)90142-3
40. (en) U. Sela, S. Ganor, I. Hecht, A. Brik, T. Miron, A. Rabinkov, M. Meir Wilchek, D. Mirelman, O. Lider and R. Hershkoviz, "Allicin inhibits SDF-1 alpha induced T cell interactions with fibronectin and endothelial celles by down-regulating cytoskeleton rearrangement, Pyk-2 phosphorylation and VLA-4 expression", Immunology. 2004;111:391-399.
DOI: 10.1111/j.0019-2805.2004.01841.X
41. (en) Lindsey J. Macpherson, Bernhard H. Geierstanger, Veena Viswanath, Michael Bandell, Samer R. Eid, Sunwork Hwang et and Ardem Patapoution. The purgency of garlic : Activation of TRpA1 and TRpV1 in response to allicin. Current Biology. 2005;15:929-934.
42. (en) Bautista DM, Movahed P, Hinman A, Axelsson HE, Sterner O, Hogestatt ED, Julius D, Jordt SE and Zygmunt PM, "Pungent products from garlic activate the sensory ion channel TRpA1", Proc Nath Acad Sci USA. 2005;102(34):12248-52
PMID 16103371
DOI 10.1073/pnas.0505356102
43. Inhibition of whole blood platelet-aggregation by compounds in garlic clove extracts and commercial garlic products, Lawson, LD, Ransom DK, Hughes BG. Throm. Res. 1992;65:41-156.
44. (en) Vipraja Vaidya, Keith U. Ingold et Derek A. Pratt, "Garlic : source of the Ultimate Antioxydants-Sulfenic Acids", Angewante Chemie, 2009;121(1):163-166 DOI 10.1002/ange.200804560, lire en ligne, consulté le 21 février 2009).
45. (en) S Ankri et D Mirelman, "Antimicrobial properties of allicin from garlic", Microbes Infect. 1999;2:125-9.
46. (en) RR Cutler et P Wilson, "Antibacterial activity of a new, stable, aqueous extract of allicin against methicilkan-resistant staphylococus aureus (fichier PDF)", British Journal of Biomedical Science, 2004;61(2):71-4 (lire en ligne)
47. (en) MA Cliff et H Heymann. Time-Intensity evaluation of oral burn. J. Sens. Stud, 1992;8:201-211.
DOI: 10.1111/j.1745-459.x.1992.tb00195.x
48. (en) S Narasimhen et VS Govindarajan Evaluation of spices and oleoresin – VI – purgency of ginger components, gingerols and shogoals and quality. International Journal of Food Science & Technology. 1978;13(1) :1-36.
DOI:10.1111/j.1365-621.1978.tb00773.x.
49. (en) VS Govindarajan, S Narasimhan, B Rajalakshmi et D Rajalakshmi. Evaluation of spices and deoresins – Correlation of pungency stimuli and pungency in ginger. Zeitschrift fur Lebensmitteluntersuchung und-Forschung A. 1980;170(3) :200-203.
DOI: 10.1007/BF01042540.
50. (en) Shoba G, Joy T, Majeed M, Rajendran R, Srinivas PS, " Influence of piperine on the pharmacokin etics of curcumin in animals and human volunteers ", Planta Med., 1998, 64(4) :353 – 6 (PMID 9619120, DOI 10.1055/s- 2006-957450).
51. Arnault I, Anger J. Seleno – compounds garlic and onion. J chromatogr A. 2006;1112(1-2):23-30
52. Burke KE, et al. The effect of topical and oral L-selenomethionine on pigmentation and skin cancer induced by ultraviolets radiation, Nutr. Cancer. 1992;17:123-37
53. Lombard K, Peffley E, et al. Quercetin in onion (*Allium cepa* L.) after heat treatment simulating home preparation. Journal of food composition and analysis 2005;18:571-581. Ref Type: Journal (Full).
54. Kawamoto E, Sakai Y, et al. Effects of boiling on the antihypertensive and antioxidant activities of onion. J Nutr Sci Vitaminol(Tokyo). 2004;50(3):171-6.
55. Graf BA, Milbury PE, Blumberg JB. Flavonols, flavones, flavanones, and human health: epidemiological evidence. J. Med Food. 2005;8(3):281-90.
56. Aviran M, Kaplan M, et al. Dietary antioxidants and paraoxonases against LDL oxidation and atherosclerosis

development. Handb Exp. Pharmacol. 2005;170:263– 300.
57. Morse R, Lisk DJ. Elemental analysis of honeys from several nations, American Bee. 1980;(7):522–523.
58. Adeny FM, et al. Chemical/ Physical characterization of Nigerian Honey. Pakistan Journal of Nutrition. 2004; 3(5):278– 281
59. Subramanian M, Sreejayan; Rao, MNA, Devasagayam TPA, Singh BB. Diminution of singlet oxygen – Induced DNA Damage by curcumin and Related Antioxidants. Fundamental and Molecular Mechanisms of Mutagenesis. 1994;311:249-255.
60. Gordon ON, Luis PB, Sintim HO, Schneider C. Unraveling curcumin Degradation. Journal of Biological Chemistry. 2015;290(8):4817-4828.
61. Dinkova – kostova AT, Massiah MA, Bozak RE, Hicks RJ, Talalay P. Potency of Michael Reaction Acceptors as Inducers of Enzymes That Protect against carcinogenesis Depends on Their Reactivity with sulfhydryl Groups. Proceedings of the National Academy of sciences of the United States of America. 2000;98(6):3404 – 3409.
62. Fang J, Lu J, Holmgren A. Thioredoxin Reductase Is Irreversibly Modified by curcumin. The Journal of Biological Chemistry. 2005;280(26):25284-25290.
63. Heger M, Van Golen RF, Broekgaarden M, Michel MC. The Molecular Basis for the Pharmacokinetics and Pharmacodynamics of curcumin and Its Metabolites in Relation to cancer. Pharmacological Reviews. 2014;66(1):222 -307.
64. Kolev TM, Velcheva EA, Stamboliysha BA, Spiteller MDFT. Experimental studies of the Structure and Vibrational Spectra of curcumin. International Journal of Quantum Chemistry 2005;102:1069 -1079.
65. Balasubramanian K. Molecular orbital Basis for Yellow curry Spice Curcumin's Prevention of Alzheimer's Disease. Journal Agricultural Food Chemistry. 2006;54(10):3512 -3520.
66. Li J, Dai C, Sum H, Jin L, Guo C, Cao W, Wu J, Tian H, Luo C, Ye W, Jiang R. Protective effects and Mechanisms of curcumin on Podophyllotoxin Toxicity *In vitro* and *In vivo*. Toxicology and Applied Pharmacology. 2012;265(2):190 – 199.
67. Bstanji Y, Taha MO, Alimasri IM, Al-Ghussein MAS, Mohammad MK, Alkhatib HS. Inhibition of Glycogen synthase Kinase by curcumin: Investigation by Simulated Molecular Docking and Subsequent in Vitro/in Vivo Evaluation. Journal of Enzyme Inhibition and Medecinal Chemistry. 2009;24(3):771 – 778.
68. Ngo ST, Li MS. Curcumin Binds to Aβ 1-40 Peptides and Fibrils Stronger Than Ibuprofen and Naproxen. Journal of Medicinal Chemistry. 2012;116:10165-10175.
69. Borsari M, Ferrari E, Grandi R, Saladini M. Curcuminoids as Potential New Iron-chelating Agents: Spectroscopic, Polarographic and Potentiometric study on Their Fe(III) Complexing Ability. Inorganica Chemica Acta. 2002;328:61-68.
70. Christelle HOMBOURGER, Thèse de doctorat : « De l'épice au médicament », Faculté de Pharmacie / Université Henri Poincaré, Nancy 1, 2010
71. Wilobon Komonsing, Sebastian Reyer, Pramote Khuwijitjaru, Busarakom Mahayothee, Joachim Muller. Drying Behavior and Curcuminoids changes in turmeric Slices during Drying under Simulated Solar Radiation as Influenced by Different Transparent Cover Materials », Foods (MDPI). 2022;11:696.
72. Hee Jeung Kim, Jungil Hong, Induction of lipid peroxidation and melanoma cell death by turmeric oleoresin through its photosensitizing properties, Korean J. Food Sci. Technol. 2022;54(1):59-65.
73. Ni Nyoman Nurdeviyanti, I Gusci Kelut Armiate, Pande Putu Levina Amanda Krisna. Efficacy of Turmeric Extract (*Curcuma domestica* Val) 40%, 50%, 60% Concentrations In Inhibiting the Growth of Streptococcus mutans bacteria, Scientific Research Journal (SCIRJ). 2021;9 (12).

WEB SOURCES

i. Available: www.atmo-aquitaine.org consulted on 22 march 2022
ii. Available: www.quebec.ca consulted on 22 march 2022
iii. Available: www.santepubliquefrance.fr consulted on 22 march 2022
iv. Available: www.conservation-nature.fr consulted on 22 march 2022
v. Available:http://www.passeportsante.net/fr/solutions/Plantes Supplements/Fiche.aspx?doc=curcuma_ps , consulted on 12 september 2009.

vi. Available: http://www.pharmacie-des-rosiers.com/uploads/file/plantes_medicinales%5B1%5D.pdf, consulted on 14 april 2010.
vii. Available: http://form-fr.desigusxpro.com consulted on 4 april 2022
viii. Available:http://www.cuisineaz.com>interne consulted on 4 april 2022
ix. Available: https://www.mr-plantes.com/2014/02/detox/ consulted on 22 january 2022

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/86276