International J. Seed Spices 10(1), January 2020:65-72

Interrelation between spices and chronic diseases: A Review

B.S.Meena[1]*, Deepa Indoria[2], R.D. Meena[3] and S.S. Meena[3]

[1]Krishi Vigyan Kendra, Hindon and [2]Krishi Vigyan Kendra, Chittorgarh and

[3]ICAR-National Research Centre on Seed Spices, Tabiji, Ajmer-305 206, India

Abstract

Several scientific studies have proved spices defensive role against chronic diseases and other diseases. In reality, spices by mean of active compounds can help in Parkinson, arthritis, neurodegenerative disorders (Alzheimer's, amyotrophic lateral sclerosis, Huntington's disease, sore muscles, diabetes, gastrointestinal problems etc. Roles of spices and their energetic components in chronic diseases (cancer, arthritis, cardiovascular diseases, etc.) and their mechanism of action have been reported by researcher. The key risk factors associated with these diseases are unhealthy lifestyle including lack of physical activity, poor diet, stress, excessive tobacco and alcohol consumption, exposure to radiations, and infection harmful pathogenic microorganisms. Nutritional biotherapy and bio therapeutics have develop into important to reverse these global diseases. Bio-therapeutics that involves Indian spice therapy requires measurement with relevance to insulin therapy, antimicrobial therapy, immune-therapy and drug therapeutics. Combined insulin therapy with Indian spice therapy tremendously regulates human insulin biological activity with significance to the prevention of uncontrolled intracellular glucose levels as well as mitochondrial apoptosis. At the present it is well proved that these agents induce inflammation and deregulate inflammatory pathways that can lead to the development of chronic diseases.

Key words : Carcinogenic, chronic disease, inflammation.

Introduction

Spices are not only considered just herbs used in culinary for getting better the taste of dishes but they are even the sources of a plentiful bioactive compounds those are significantly beneficial for human health. Spices is a broad group that may include numerous herbs and other plant like turmeric, chilli, cardamom, pepper, clove, zinger, coriander, cumin, fenugreek, fennel, dill, anise, ajowain, mint, nigella, celery, rai, cinnamon, nutmeg, garlic, onion etc. Spices have been used since ancient times due to their fragrance, antimicrobial, anti-inflammatory and carminative properties. Initially dill (*Anethum sowa* L.) a spice was used for flavoring in dynastic Egypt and for flavoring and medicine by the Greeks and Romans (Meena *et al*., 2013). Total approximately 106 spices are cultivated in world out of which India grows more than 60 spices (Meena *et al*., 2014). Fennel is cultivated throughout the temperate and sub tropical region in the world mainly in Romania, Russia, Hungary, Germany, France, Italy, India, Srilanka, Malaysia, Japan, Argentina and USA (Meena *et al.,* 2017). Bio-therapeutics have become an importance way to the global chronic diseases to stop accelerated aging linked with uncontrolled immune reactions with the intention of determine treatment and disease development. Collective insulin therapy with Indian spice therapy tremendously regulates human insulin's biological activity with significance to the prevention of uncontrolled intracellular glucose levels. At the present it is well proved that these agents induce inflammation and deregulate inflammatory pathway, which can lead to the development of chronic diseases Inflammation, that means, "to set on fire" a body's natural response against pathogen, such stimuli occurs in two different stages namely, acute inflammation and chronic inflammation. Acute inflammation is a part of innate immunity initiated by the immune cells that persists only for a short time while chronic inflammation remains long. Overall, it is evident from these studies that the allure of spices is attributed not only to their aroma, but also more importantly, to their wellness power. The spice-derived compounds can interact with multiple targets and alter the deregulated inflammatory pathways and mediators associated with chronic diseases. Hence, with the fatal side effects and inflating cost of modern therapeutics, spices and their active components hold a huge guarantee for the development of affordable, novel and safe drugs against chronic diseases. However, in-depth scientific investigations are required to completely determine the potential of the spice-derived nutraceuticals and open new avenues for the better management of patients with

*Corresponding author email: bs_meena38@yahoo.com

chronic diseases. Factors such as stress, core body temperature and food quality influence bio-therapeutics and Indian spice therapy with delayed spice clearance associated with mitochondrial dysfunction (cell apoptosis) and altered drug/caffeine therapy with relevance to the global diabetes pandemic (Martins, 2018). Further, foods that contain essential nutrients consist of protein, eggs, cottage cheese, dairy, red meat, chicken, legumes, duck, nuts, and seeds. These essential nutrients comprise methionine, methylsulfonylmethane, sulphur, choline, and trimethylglycine as building blocks that allow regulation of genes by appropriate telomeres. Vitamins such as vitamin B12, folic acid, and vitamin B6 play multiple role. Biotherapeutics with nutritional biotherapy involve the use of various nutrients such as magnesium and phosphatidylinositol (gm day^{-1}) are essential to maintain genes involved in insulin therapy.

Spices therapy for chronic diseases

In the global burden of disease connections between nutritional therapy and the immune system have become of medical interest with primary immune dysregulation associated to obesity, diabetes and neurodegenerative diseases (Martins, 2015; Martin, 2017).

They are also sources of a numerous bioactive compounds significantly beneficial for health (Bukvicki *et al.,* 2018). Since time immemorial, photochemical, both in their natural as well as synthetic forms have been used for the treatment of various chronic diseases the root, leaf, bud, seed, bark, berry, stigma of a plant or flower used for the culinary purpose are generally called as spices. Spices not only add flavour and taste to food, but also exhibit tremendous health benefits. Numerous results from preclinical and clinical studies over the past several decades have ascertained the efficacious role of spices and their active components in preventing and combating various diseases including arthritis, asthma, cancer, cardiovascular diseases, diabetes, and neurodegenerative diseases. Nutrition is very much essential to reduce diseases relevant to community factors and global antibiotic resistance (Larson, 2007; Martins, 2017). Nutritional diets are indispensable to maintain immunotherapy and antimicrobial therapy (Martins, 2015; Martins, 2016; Martins, 2017). Drug biotherapeutics is essential to stabilize chronic disease with dietary involvements and fat consumption that determine biotherapeutics significant to the treatment of endocrine and metabolic diseases (Martins, 2018). Nutritional interventions with Indian spices and insulin therapy have become now importance in the world for diabetic pandemic with human insulin and its biological activity (Martins, 2017; Martin, 2018). Indian spices have been reported to exhibit a broad range of physiological and pharmacological properties that create beneficial health promoting and protective effects for various chronic diseases (Krishnaswami, 2008; Sun *et al*., 2014). Indian spices as a biotherapy have become important in the developed and developing world with specific spices such as cinnamon and curcumin involved in the control of the immune system and the antimicrobial therapy (Nabavi *et al.,* 2015; Roth *et al*., 2014; Gunes *et al.,* 2016; Bose *et al*., 2015).

Several other spices such as saffron, curcumin, pepper, zinger and cinnamon has been used for the treatment of hypercholesterolemic, obesity, cardiovascular disease, inflammation, metabolic disease, diabetes and Alzheimer's disease (Krishnaswami, 2008; Sun *et al*., 2014). (Martins, 2018) reported the cinnamon and curcumin as nutritional interventions have major effects on drug and hormone biotherapy with doses of these spices important to determine stabilization and reversal of global chronic disease. Insulin therapy is one of the most important treatments in diabetes with Figure 1. Biotherapeutics and nutritional biotherapy have become important to reverse global diseases such as non alcoholic fatty liver disease (NAFLD), diabetes and neurodegenerative diseases. Biotherapeutics that involve Indian spice therapy require assessment with relevance to immunotherapy, antimicrobial therapy and drug therapeutics. Diabetes and mitochondrial dysfunction are closely connected with Indian spice and Insulin therapy to be carefully assessed with relevance combined therapy and increased cellular glucose levels related to hyperglycemic mitochondrial apoptosis (Cai *et al*., 2002). Indian spices (curcumin) as a biotherapy in health and disease should be carefully controlled with higher doses that not associated with activation of anti-aging genes involved in mitochondrial biogenesis (Martins, 2016). Biotherapeutics for diseases are now ineffective with malfunction of nutrient sensitive genes involved in mitochondrial survival (Martins, 2018; Cai *et al*., 2002). Cinnamon and curcumin involved in the improvement of plasma hyperglycemia and involved with the regulation of insulin dose/type and frequency of use in diabetes therapeutics (Qin *et al*., 2010; Jimenej-Osorio *et al*., 2016; Chuengsamarn *et al*., 2012). Curcumin effects on the insulin receptor and beta cell function modulates human insulin therapy with critical consideration of Indian spice therapy required with relevance to human insulin administration and diabetes treatment (Vantyghem, 2014). Martins (2018) reported the key role of spices in maintaining genomic stability as spices are rich in

antioxidants as well as vitamins C, D and E.

Biotherapeutics that involves caffeine has been extensively studied in obesity and diabetes with curcumin doses and caffeine intake important to hyperglycemia induced cell apoptosis (Lane, 2004). Indian spices that induce cell apoptosis prevent cancer include curcumin (turmeric) and piperine (black pepper) with interference with caffeine metabolism and active spice component pharmacokinetic data is still not available (Zheng, 2016; Kaefer, 2011; Alam, 2015). Cinnamon has been shown to regulate insulin levels with therapeutic effects on hyperglycemia induced mitochondrial apoptosis (Anderson *et al.*, 2015). Factors such as core body temperature and stress may override Indian spice therapy and various biotherapeutics that are of prime importance in the stabilization of the global chronic disease epidemic (Martins, 2015). Core body temperature connections to the immune system and mitochondrial cell function indicate that with heat/cold stress induce toxic immune reactions that are relevant to mitochondrial apoptosis in non alcoholic fatty liver disease, obesity, diabetes and neurodegenerative diseases (Martins, 2018). Indian spice therapy reduces aging process but at higher doses of them are therapeutic for cancer treatment with relevance to induction of cell apoptosis (Cai *et al.*, 2002). Furthermore diets and foods that contain Indian spices may alter the apelinergic system involved in stress reactions, co-ordination of the neuroendocrine system and the development of chronic disease (Martins, 2015). The most commonly used spices for culinary purpose that shows biological activities are black pepper, cardamom, cinnamon, clove, cumin, fenugreek, fennel, garlic, ginger, onion, rosemary, turmeric etcTurmeric (*Curcuma longa*) is the most commonly used spice in the world. Curcumin, the main component of turmeric (2–5%), obtained from rhizomes of this plant, is a yellow colored compound, which gives the golden color to turmeric, was first isolated by Vogel in 1842.

In 1910, the structure of curcumin was determined as diferuloylmethane and later synthesized and cocrystallized with 5-LOX in 2003 this 'golden spice' is recognized for its anti-inflammatory, antimicrobial, insecticidal, antimutagenic, radioprotective, and anticancer properties. Over ten thousand studies have been reported in the literature about the biological activities of this compound including more than 120 clinical trials. Besides curcumin, the other active components of turmeric include demethoxycurcumin, bisdemethoxycurcumin, sesquiterpenes, diterpenes, triterpenoids. Black pepper (*Piper nigrum)*, another commonly used spice is widely known for its immunomodulatory, anti-oxidant, anti-asthmatic, anti-carcinogenic, anti-inflammatory and anti-ulcer properties Other than its main component piperine, black pepper also contains β-caryophyllene, limonene, δ-3-carene, α-pinene, β-pinene, α-phellandrene, myrcene, terpinolene, etc. Another extensively used spice, ginger (*Zingiber officinale*) is reported to have different biological properties such as antioxidant, anti-inflammatory and antiproliferative properties. Table No. 1 shows a list of spices, their common names, scientific names, and their active components.

Active components of spices

Increasing lines of evidence have established the efficacy of the principal components of spices in preventing as well as alleviating different types of chronic diseases. The main components of spices and their curative potentials are discussed below: 1,8-Cineole, 1,8-Cineole (Cin) is a monoterpene oxide found in variety of spices such as basil, cardamom, and sage. Cin has been used to treat multiple inflammatory disorders such as bronchitis, sinusitis, chronic rhinitis, and asthma. Cin has been shown to down regulate NOS-2, COX-2, and NF-κB, hence showing its potential as an anti-inflammatory agent Moreover, Cin also attenuated the colonic damage in trinitrobenzene sulfonic acid (TNBS)-induced colitis in rats; decreased acute pulmonary inflammation in vivo; ameliorated acute pancreatitis in vivo via downregulation of cytokines, oxidative stress and NF-κB. In AD, insoluble amyloid β deposits induced inflammation.

6-Gingerol

6-Gingerol, the main active component of ginger, is shown to possess different biological activities such as anti-oxidative, anti-inflammatory and anti-proliferative properties Its therapeutic effect was observed against various chronic diseases such as AD, colorectal cancer and diabetes . For example, 6-Gingerol can induce downregulation of inflammatory cytokines such as monocyte chemoattractant protein-1 (MCP-1), TNF-α, and IL-6, and NF-κB thereby, ameliorating steatohepatitis in vivo 6-gingerol also has a protective role against colitis in vivo through the activation of adenosine monophosphate-activated protein kinase (AMPK) pathway. Zingiber and cinnamon has been used for the treatment of hypercholesterolemic, cardiovascular disease, obesity, inflammation/metabolic disease, diabetes and Alzheimer's disease (Sun *et al.,* 2014).

α-Pinene

α-Pinene is a monoterpene, found mainly in eucalyptus oils and oils of aromatic plants such as rosemary. It is known to possess antimicrobial, apoptotic, antimetastatic,

Table 1. Spices and their major components

Spice name	Scientific name	Major components
Anise	*Pimpinella anisum*	Anethole, estragole, γ-hymachalen, para-anisaldehyde, methyl cavicol
Asafoetida	*Ferula asafetida*	Ferulic acid, umbel-liferone, asaresinotannols, farnesiferols A, B, C, glucose, galactose, l-arabinose, rhamnose, glucuronic acid, 2-butyl propenyl disulfide
Basil	*Ocimum basilicum*	Estragole, linalool, 1, 8-cineole, eugenol, methyl cinnamate, α-cubebene, α-farnesene, caryophyllene, β-ocimene
Bay leaves	*Laurus nobilis*	1,8-cineole, α-pinene, limonene, alpha-terpinyl acetate, terpinene-4-ol
Black cumin	*Nigella sativa*	Thymoquinone, cuminaldehyde, γ-terpinene, β-pinene, *p*-cymene, *p*-mentha-1,3-diene-7-al, *p*-mentha-1,4-dien-7-al
Black pepper	*Piper nigrum*	Piperine, β-caryophyllene, limonene, δ-3-carene, α-pinene, β-pinene, α-phellandrene, myrcene, terpinolene
Cardamom	*Elettaria cardamomum*	1,8-cineole, α-terpinyl acetate, limonene, linalool, terpinolene, myrcene, linalyl acetate
Celery seed	*Trachyspermum ammi*	2 Isopropyl-5-methyl-phenol, octadecanoic acid, lupeol acetate, hexadecanoic acid, (3β, 24S)-stigmast-5-en-3-ol, stigmasta-5,22-dien-3β-ol, lup-20(29)-en-3-yl acetate
Cinnamon	*Cinnamomum zeylanicum*	Cinnamaldehyde, cinnamyl acetate, cineole, eugenol, coumarin, linalool, humulene, ethyl cinnamate, β-caryophyllene, τ-cadinol
Clove	*Syzygium aromaticm*	Eugenol, eugenyl acetate, α-humulene, β-caryophyllene
Coriander	*Corriandrum sativum*	Petroselinic acid, linoleic acid, oleic acid, palmitic acid, stearic acid, vaccenic acid, myristic acid
Dill	*Anethum graveolens*	α-Phellandrene, limonene, dill ether, sabinene, α-pinene, *n*-tetracosane, neophytadiene, *n*-docosane, *n*-tricosane, *n*-nonadecane, *n*-eicosane, *n*-heneicosane, β-myrcene, α-tujene
Fennel	*Foeniculum vulgare*	Estragole, trans-anethole, fenchone, limonene, anisaldehyde, sabinene, β-myrcene, α-pinene, β-pinene, camphene
Fenugreek	*Trigonella foenum-graecum*	Diosgenin, yamogenin, gitogenin, tigogenin, neotigogens, carpaine, trigonelline, gentianine, 4-hydroxyisoleucine, fenugreekine, choline
Garlic	*Allium sativum*	Diallyl sulfides, diallyl disulfides, diallyl trisulfide, ajoene, allicin, alliin, methiin, S-allylcysteine, isoalliin, cycloalliin, S-allylmercaptocysteine
Ginger	*Zingiber officinale*	[6]-gingerol, [6]-paradol, shogoal, 6-gingerdiol, gingerdione, zingiberene, citral (neral and geranial), bisabolene, α-farnesene, β-phellandrene, cineole, zingerone
Kokum	*Garcinia indica*	Garcinol, xanthochymol, isoxanthochymol, 1,2 dihydroxypropane - 1,2,3-tricarboxylic acid
Mint	*Mentha* spp.	Carvone, limonene, 1, 8-cineole
Mustard	*Sinapis alba*	Allyl isothiocyanate, phenethyl isothiocyanate
Nutmeg	*Myristica fragrans*	Eugenol, methyleugenol, methylisoeugenol, elemicin, myristicin, safrole
Cumin	*Cuminum cyminum*	Cuminaldehyde, cuminol (Meena *et al.,* 2018)

and antibiotic properties á-pinene is one promising agent for treatment of various inflammatory diseases as it has been found to suppress MAPKs and NF-κB pathway. The inflammation associated with acute pancreatitis is considerably reduced by treatment with α-pinene in vivo via the downregulation of TNF-α, IL-1β, and IL-6.

Curcumin

Curcumin, an active component of turmeric, is the most widely studied nutraceutical. It is known to possess anti-antioxidant, anti-bacterial, anti-cancer, anti-fungal, anti-inflammatory and anti-viral activities. Thus, it is a potential agent against various chronic illnesses. It has been shown to modulate various inflammatory mediators including IL-6, TNF-α, PI3K/Akt, STAT3, IL-27, NF-κB, MAPK, etc. in various preclinical and clinical studies. Nabavi, (2015) has reported the curcumin is involved in the control of the immune system and the antimicrobial therapy.

Diosgenin

Dysgenic is a bioactive compound obtained from the spice *Trigonella foenum-graecum* L. (fenugreek). Over the years, this spice has been known for its anti-carcinogenic, anti-diabetic, anti-oxidant, hypocholesterolemic and immunological properties. Because of its anti-inflammatory activities, diosgenin is a potential agent for various chronic diseases including AD, breast cancer, chronic myeloid leukaemia, and osteoarthritis

Capsaicin

Aforementioned, capsaicin (trans-8-methyl-*N*-vanillyl-6-nonenamide) is a principal component of the spice red pepper (*Capsicum*) It is highly efficacious in ameliorating several chronic diseases such as asthma, diabetes, cancers of breast, cervical, stomach, etc. via the inhibition of STAT3, NF-κB, PGE2, IL-6, TNF-α, etc. (Fig. 2). Additionally, capsaicin also exhibits anticancer activity against cancer of the colon, lung, prostate, skin and tongue.

Cumim-aldehyde

The flavoring property of cumin is because of aromatic essential oil, which can be easily steam distilled *in vitro*. The main ingredient of cumin oil is 'cumin aldehyde', which shows pesticidal activity particularly antifungal (Meena *et al.,* 2018). The similar anti-fungal substance in cumin oil was also reported, that inhibits the growth of *Fusarium oxysporum*, a fungus responsible for wilt disease in several crops (Agrawal and Gour, 1992). Cumin seeds have an aromatic fragrance due to an alcohol, cuminol. Cumin is produced in Iran, Lebanon, Cypress, Egypt, India, Syria, China, Indonesia, Mexico and Argentina.

Eugenol

Eugenol, the active principle from clove extract, is well known for its anti-inflammatory properties via modulation of inflammatory biomarkers such as TNF-α, IL-1, IL-6, COX-2, PGE2, NF-κB, etc. In addition, it has been shown to inhibit various chronic diseases in preclinical studies. For instance, eugenol was shown to restrict the progression of asthma in vivo by inhibition of NF-κB pathway. This compound also inhibited cell proliferation in gastric cancer in vivo by suppressing NF-κB pathway Eugenol was found to enhance the efficacy of anti-cancer drug, gemcitabine and exert anti-inflammatory activity in human cervical cancer cells.

Garcinol

Garcinol is a polyisoprenylated benzophenone isolated from the plant *Garcinia indica* (Kokum). A functional investigation has revealed the anti-carcinogenic, anti-inflammatory and anti-oxidative properties of garcinol Studies showed that garcinol inhibited the proliferation of breast cancer cells in vitro Additionally, it also sensitized breast cancer cells to a chemotherapeutic agent, taxol via downregulation of NF-κB/Twist1 and caspase-3/iPLA(2) signalling pathways in a mouse 4T1 breast tumour model.

Conclusions

Biotherapeutics for chronic diseases has accelerated to prevent the progression of the current global chronic disease epidemic. Indian spice are known for antioxidants hence, Indian spices therapy has become an important biotherapeutic involved in the reversal of global diabetes and neurodegeneration. Mitophagy in chronic disease requires attention with Indian spice therapy and insulin therapy as a combined therapy to regulate cell glucose levels to prevent hyperglycemic induced mitochondrial apoptosis. Specific nutrients need to be consumed with Indian spices to allow stabilization of uncontrolled toxic reactions that lead to cell death. Core body temperature, stress and inappropriate food quality will inactivate Indian spice therapy with excessive Indian spice intake over many years that may be connected to ineffective human insulin biological activity/drug biotherapeutics with long term Indian spice use more relevant to cell apoptosis and the treatment of cancer. Spices are rich in antioxidants as well as vitamins C, D and E are essential and maintain genomic stability. A lack of antioxidants leads to increased free radical damage and more risk for damage to telomeres essential to cell survival. Minerals such as magnesium and zinc are required for the prevention of DNA strand breakage and the prevention of accelerated cell aging. Nutrients such as quercetin, green tea catechins, grape seed extract, resveratrol and omega 3 fatty acids (eicosapen-taenoic acid/docosahexaenoic acid) are

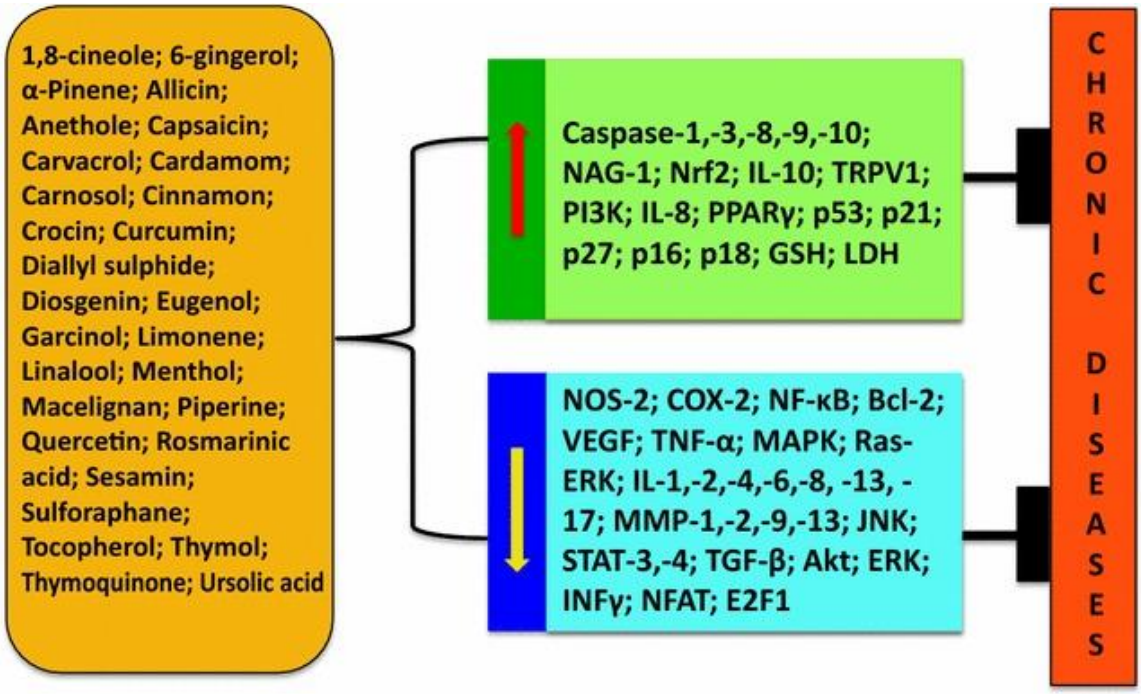

Fig. 1. Different bioactive components of spices and their molecular mechanisms against different chronic diseases

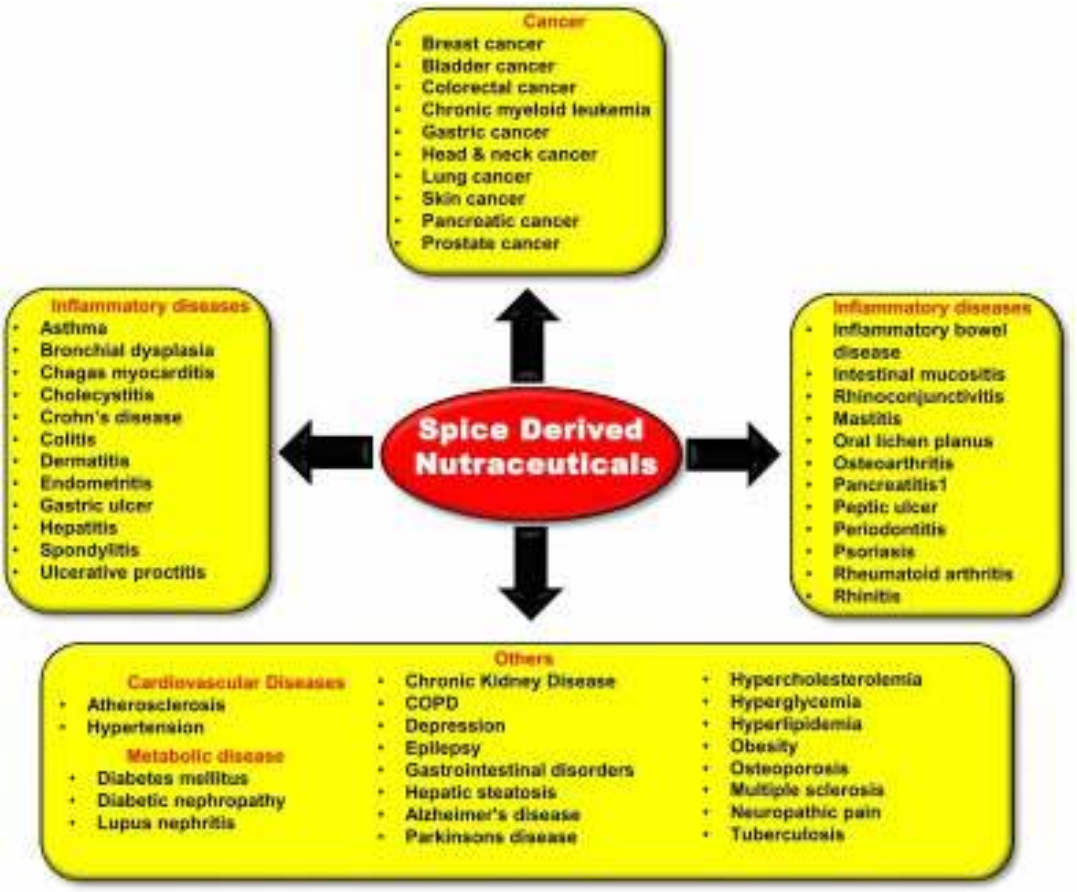

Fig. 2. Spice derived nutraceuticals against various chronic diseases

important as basic nutrients to preserve biological aging and reverse diabetes.

References

Alam, I., Imam, H. and Riaz, Z. 2015. Cancer preventing spices. *J. Cancer Metastasis and Treatment,* 1, 41-42.

Anderson, R.A., Zhan, Z., Luo, R., Guo, X., Guo, Q., Zhou, J., Kong, J., Davis, P.A. and Stoecker, B.J. 2015. Cinnamon extract lowers glucose, insulin and cholesterol in people with elevated serum glucose. *J. Traditional and Complementary Medicine*, 6: 332-336.

Bose, S., Panda, A.K., Mukherjee, S. and Sa, G. 2015. Curcumin and tumor Immune- editing: resurrecting the immune system. *Cell Division*, 10, 6. https://doi.org/10.1186/s13008-015-0012-z

Bukvicki, D., Gottardi, D., Prasad, S., Novakovic, M., Marin, P., Tyagi, A.K. 2018. The healing effects of spices in chronic diseases. *Curr Med Chem.* doi: 10.2174/0929867325666180831145800

Cai, L., Li, W., Wang, G., Guo, L., Jiang, Y. and Kang, Y.J. 2002. Hyperglycemia- induced apoptosis in mouse myocardium: mitochondrial cytochrome C-mediated caspase-3 activation pathway. *Diabetes*, 51,1938-1948.

Chuengsamarn, S., Rattanamongkolgul, S., Luechapudiporn, R., Phisalaphong, C. and Jirawatnotai, S. 2012. Curcumin extract for prevention of type 2 diabetes. *Diabetes Care* , 35, 2121-2127. https://doi.org/10.2337/dc12-0116

Gunes, H., Gulen, D., Mutlu, R., Gumus, A., Tas, T. and Topkaya, A.E. 2016. Antibacterial effects of curcumin: An *in Vitro* minimum inhibitory concentration study. *Toxicology and Industrial Health*, 32, 246-250.

Jiménez-Osorio, A.S., Monroy, A. and Alavez, S. 2016. Curcumin and insulin resistance-molecular targets and clinical evidences. *Biofactors*, 42, 561-580. https://doi.org/10.1002/biof.1302.

Kaefer, C.M. and Milner, J.A. 2011. Herbs and spices in cancer prevention and treatment. In: Benzie, I.F.F. and Wachtel-Galor, S., Eds., Herbal Medicine : Biomolecular and Clinical Aspects , 2nd Edition, CRC Press/Taylor & Francis, Boca Raton.

Krishnaswamy, K. 2008. Traditional indian spices and their health significance. *Asia Pacific J. Clinical Nutrition*, 217, 265-268.

Lane, J.D., Barkauskas, C.E., Surwit, R.S. and Feinglos, M.N. 2004. Caffeine impairs glucose metabolism in type 2 diabetes. *Diabetes Care* , 27, 2047-2048.

Larson, E. 2007. Community Factors in the development of antibiotic resistance. *Annual Reviews in Public Health*, 28, 435-447.

Martins, I.J. 2015. Nutritional diets accelerate amyloid beta metabolism and prevent the Induction of chronic diseases and alzheimer's disease. Photon ebooks, 1-48.

Martins, I.J. 2015. Over nutrition determines LPS regulation of mycotoxin induced neurotoxicity in neurodegenerative diseases. *International J. Molecular Science*, 16, 29554-29573.

Martins, I.J. 2015. Unhealthy nutrigenomic diets accelerate NAFLD and adiposity in global communities. *J. Molecular and Genetic medicine*, 9, 1-8.

Martins, I.J. 2016. Anti-aging genes improve appetite regulation and reverse cell senescence and apoptosis in global populations. *Advances in Aging Research*, 5, 9-26. https://doi.org/10.4236/aar.2016.51002.

Martins, I.J. 2016. Food and nutrition cause liver and brain diseases. https://atlasofscience.org/food-and-nutrition-cause-liver-and-brain-diseases-with-d iabe.

Martins, I.J. 2017. Antibiotic resistance involves antimicrobial inactivation in global communities. *Scholarena J. Pharmacy and Pharmacology*, 2, 1-3.

Martins, I.J. 2017. Antimicrobial activity inactivation and toxic Immune eeactions induce epilepsy in Human. *J. Medical Discovery*, 2, 1-7.

Martins, I.J. 2017. Appetite control and nutrigenomic diets are connected to immune regulation and diabetes prevention. EC Nutrition, 12, 120-123.

Martins, I.J. 2017. Autoimmune disease and mitochondrial dysfunction in chronic diseases. *Research on Chronic Disease*, 1, 10-12.

Martins, I.J. 2017. Insulin therapy inactivation is connected to NAFLD and diabetes severity index. *J. Diabetes and Clinical Studies*, 1, 1-3.

Martins, I.J. 2018. Indian spices and unhealthy diets interfere with drug therapy in diabetes and neurodegenerative diseases. *Novel Approaches in Drug Designing and Development*, 3, 1-4.

Martins, I.J. 2018. Indian spices and biotherapeutics in health and chronic disease. *Health*, 2018, 10, 374-380

Meena, S.S., Singh, B., Singh, D., Ranjan, J.K. and Meena, R.D. 2014. Pre and post harvest factors effecting yield and quality of seed spices: A review. *International J. Seed Spices,* 3(1): 1-11.

Meena, S.S., Mehta, R.D. Meena, Meena, N.K. and Singh, B. 2014. Pre and post harvest factors effecting yield and quality of seed spices: A review. *International J. Seed Spices,* 3(1): 1-11.

Meena R.D., Singh, R., Lal, G., Sharma, Y.K., Kumar, N., Meena, N.K., Meena, S.S., Meena, N.L., Choudhary, S. and Verma, A.K. 2017. Effect of weed invasion on *Ramularia* blight disease incidence in fennel (*Foeniculum valgare* Mill.). *International J. Seed Spices,* 7(1):65-67.

Meena, R.D., Lal, G., Mehta, P., Sharma, Y.K., Meena, S.S., Meena, R.S., Meena, N.K., Mishra, B.K., Meena, R.L., Meena, N.L. and Tripathi, G.K. 2018. Efficacy of soil solarization on growth and yield of cumin (*Cuminum cyminum* L.) under arid conditions. *International J. Seed Spices,* 8(1): 74-79

Nabavi, S.F., Lorenzo, A.D, Izadi, M., Sobarzo-Sánchez, E., Daglia, M. and Nabavi, S.M. 2015. Antibacterial Effects of cinnamon: from farm to food, cosmetic and pharmaceutical industries. *Nutrients*, 7, 7729-7748.

Qin, B., Panickar, K.S. and Anderson, R.A. 2010. Cinnamon: Potential role in the prevention of insulin resistance, metabolic syndrome, and type 2 diabetes. *J. Diabetes and Science Technology*, 4, 685-693.

Roth-Walter, F., Moskovskich, A., Gomez-Casado, C., Diaz-Perales, A., Oida, K., Singer, J., Kinaciyan, T., Fuchs, H.C. and Jensen-Jarolim, E. 2014. Immune suppressive effect of cinnamaldehyde due to inhibition of proliferation and induction of apoptosis in immune cells: implications in cancer. *PLoS ONE*, 9, e108402. https://doi.org/10.1371/journal.pone.0108402.

Sun, D., Lv, J., Chen, W., Li, S., Guo, Y., Bian, Z. 2014. Spicy food consumption is associated with adiposity measures among half a million chinese people: The China Kadoorie Biobank Study. BMC Public Health, 14, 1293. https://doi.org/10.1186/1471-2458-14-1293.

Vantyghem, M.C., Defrance, F., Quintin, D., Leroy, C., Raverdi, V. and Prévost, G. 2014. Treating diabetes with islet transplantation: lessons from the past decade in lille. *Diabetes and Metabolism*, 40, 108-119. https://doi.org/10.1016/j.diabet.2013.10.003

Zheng, J., Zhou, Y., Li, Y., Xu, D.-P., Li, S. and Li, H.-B. 2016. Spices for prevention and treatment of cancers. *Nutrients*, 8, E495. https://doi.org/10.3390/nu8080495.

Received : November 2019; Revised : December 2019; Accepted : December 2019.