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Study of Capsaicinoids in Chillies & Its Therapeutic Applications

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Abstract: Bioactive natural products are the main sources of new drugs, functional foods and food additives. Chilli is one of the important plants used worldwide as a vegetable, a spice and an external medicine. Capsaicinoids, the spice element present in chillies, is one of the best – known natural compounds. The extraction of the capsaicinoids can be executed in many ways such as Maceration method, Soxhlet method and Hydro – distillation method, with different types of organic solvents, but the yield varies with the variety of chillies used. Also, the amount of capsaicinoids present in the chilli fruit is quantified by organoleptic, spectrophotometry, thin – layer chromatography, gas chromatography and high – performance liquid chromatography methods. In this review, we will have a look at the different types of capsaicinoids present in chillies, its extraction and the numerous applications of it.

Index Terms **– Capsaicinoids, chillies, ointment, pepper spray, dermal patch.**

I. INTRODUCTION

Chilli is one the most important and frequently used ingredients in any type of food. It has various parts namely the pedicel, calyx, seeds, placenta, capsaicin glands, pericarp, apex and locules. The pedicel is the small stem which attaches the fruit (chilli) to the plant. If a branch has many pedicels, then that branch is called the peduncle. The calyx connects the pedicel to the fruit. It looks like a hat covering the fruit. The outer part of the calyx is the sepal, it protects the flower. The seeds are the reproductive part of the plant. They contain less amount of capsaicin as compared to the placenta. The placenta is where the seeds of the fruit are attached. Between the seeds and the placenta there is a thin layer which is called the capsaicin gland. It is responsible for the chilli to be spicy. The pericarp is the wall of the fruit. It consists of three layers. The shiny outermost layer is the exocarp, it is a protective layer. Below the exocarp is the mesocarp which provides structural support to the fruit and holds the maximum amount of water present in the fruit. The last and the innermost layer is the endocarp, a thin, membranous layer that encloses the placenta and seeds. The chamber that contains the seeds is called the locules, some chillies have four locules while some have only one locule. The last tip of the chilli is the apex. It has the least amount of capsaicin present in it. Capsaicinoid in chillies make the chillies spicy. It is an ingredient important in the food and pharmaceutical industries. Therefore, many researchers are engaged in improving its production be it by manipulating the chilli plant cultivation conditions, chemical synthesis, enzymatic synthesis or alternative methods such as cell or tissue culture. Till date, research has shown that capsaicinoids have a wide range of biological and physiological activities which provide them functions such as antioxidants, anti – carcinogenic, promotion of energy metabolism and suppression of fat accumulation and anti-inflammatories [2, 5].

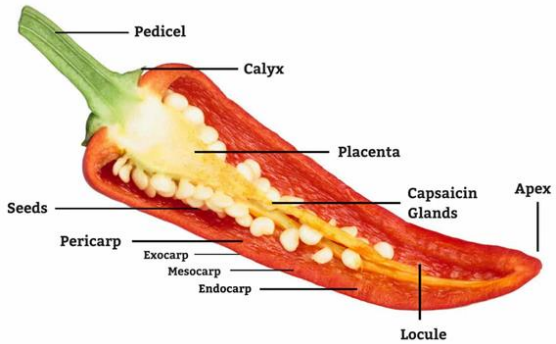
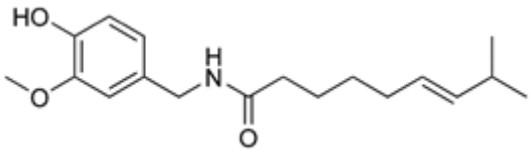
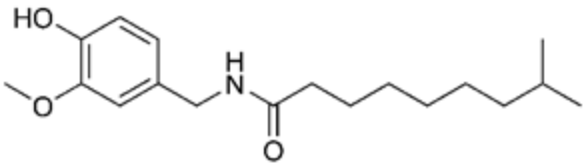
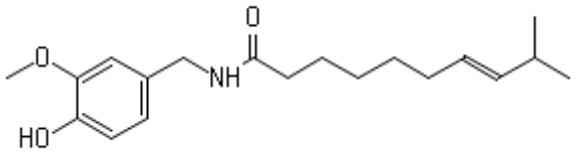
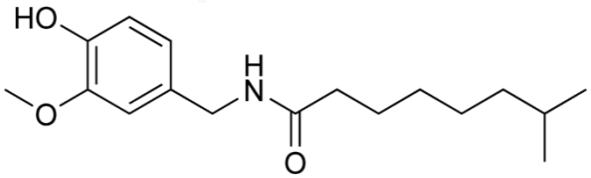
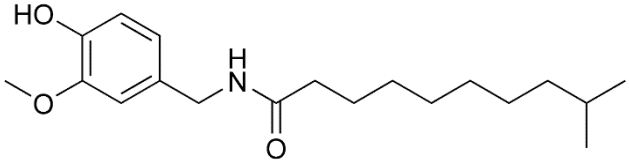


Figure 1 The Various Parts of a Chilli

II. WHAT ARE CAPSAICINOIDS?

Capsaicinoids belong to the family of secondary plant non – toxic alkaloid metabolites that are present in chillies. It gives the chilli a spicy flavour. The primary capsaicinoid present in chilli is capsaicin, it is followed by dihydrocapsaicin, nordihydrocapsaicin, homodihydrocapsaicin and homocapsaicin. Capsaicin and dihydrocapsaicin account for approximately 90% of the total capsaicinoids present. Capsaicin (trans-8-methyl-N-vanillyl-6-nonenamide) ($C_{18}H_{27}NO_3$) is a crystalline, lipophilic, colourless and odorless alkaloid. Its molecular weight is 305.40 g/mol, and it is fat, alcohol and oil-soluble. Tresh crystallized capsaicin in 1876, he was the one who named it. The molecular structure was resolved by Nelson and Dawson in 1919 [2].

Table 1 Different Types of Capsaicinoids [1]

Compounds	Structure
Capsaicin	
Dihydrocapsaicin	
Homocapsaicin	
Nordihydrocapsaicin	
Homodihydrocapsaicin	

The biosynthesis pathway of capsaicin is distinguished into two paths (figure 2). One runs through the branched fatty acid moiety derived from L-valine. The second is the synthesis of vanillylamine moiety via phenylpropanoid shikimate/arogenate [5].

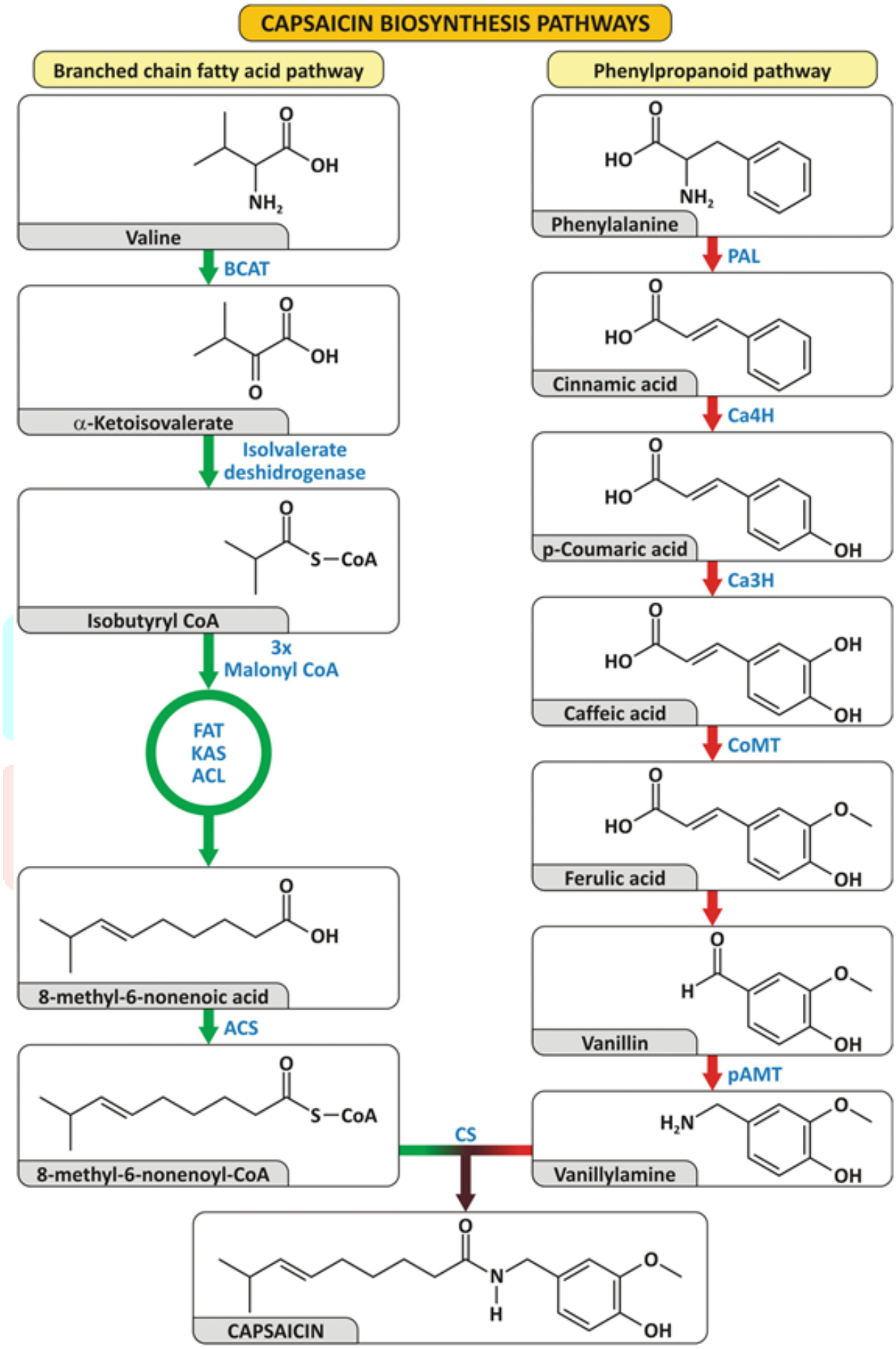


Figure 2 Biosynthesis Pathway of Capsaicin [3]

III. CAPSAICINOID EXTRACTION

The extraction of capsaicinoids from chillies is usually performed using organic solvent such as methanol, acetone, acetonitrile and chloroform. The amount of capsaicinoids extracted varies according to the various types of chillies and the pre – extraction process. Research suggests that ethanol and acetonitrile are better solvents for extraction of capsaicinoids from the fresh chillies whereas acetone is a better solvent for the dried chillies. A number of techniques are used for the extraction of capsaicinoids, the traditional ones are Maceration method, Soxhlet method and Hydro – distillation method. In the maceration method, the sample (for example chilli) is immersed into an organic solvent (ethanol) and is stirred every day for the next five to six days. The capsaicin present in the chilli will get dissolved into the ethanol and then the mixture can be placed in a rotavapor to get the capsaicin concentrate. The advantage of this method is that there is complete extraction of the material required, there is lower chemical modification of the extract, low cost and better homogeneity. In the soxhlet method, the extraction solvent is continuously passed through the soxhlet extractor by boiling and condensing. This method is mostly used in laboratories where the extract extracted can be of less quantity and also the solvent used can be recycled. The last method is the hydro – distillation method which uses a Clevenger apparatus or is done by steam distillation. Here, the sample is hydrated and distilled, then vapour phase is condensed to obtain the pure extract. The setup is very simple and the solvent used is mostly inorganic which makes it a cheap process [1, 4].

Figure 3 Rotavapour used in Maceration Method

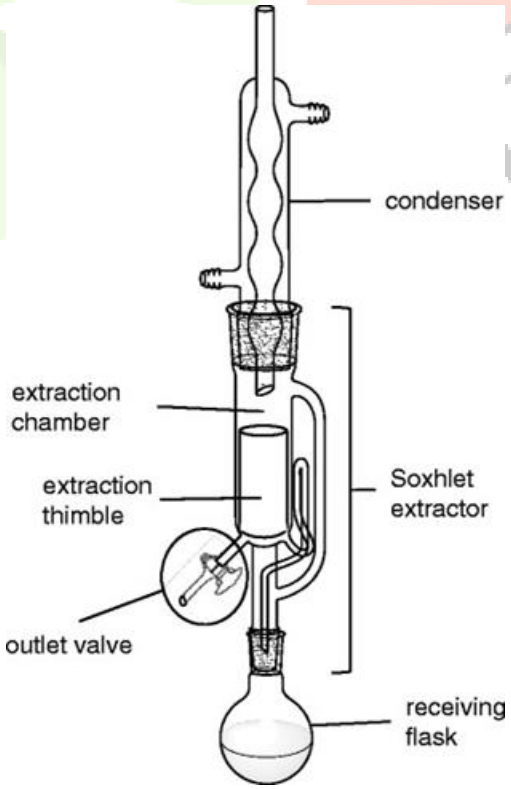


Figure 4 Soxhlet Extractor

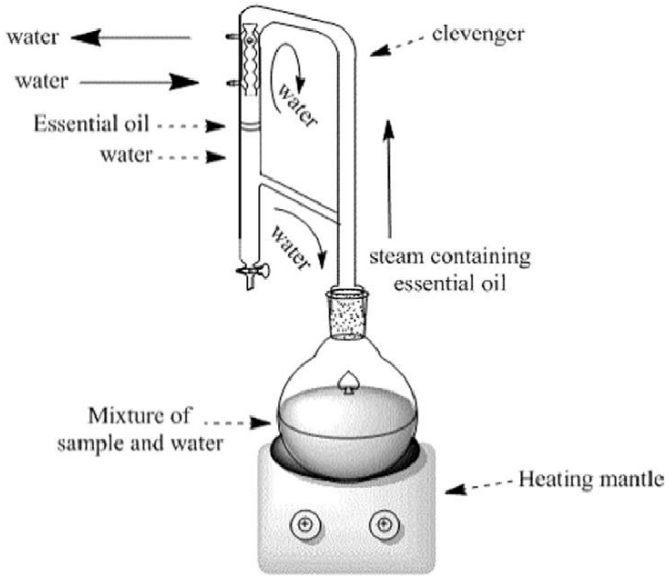


Figure 5 Hydro – Distillation Clevenger Apparatus

IV. Applications of Capsaicinoids

4.1 Tear Gas and Pepper Spray

Tear gas and pepper spray are known as riot control agents or harassing agents. They were initially used by the military in warfare. They are now used for personal protection and by enforcement agencies as a non-lethal option for subduing combative subjects and in crowd control. Pepper spray and other tear gases are classified as lachrymatory agents. Lachrymatory agents attack the mucous membranes. This causes acute eye pain, tearing, respiratory tract irritation and skin irritation. The active agent in pepper spray and tear gas, Oleoresin capsicum (OC), is the oily concentrated extract from the chili peppers. Pepper spray works almost instantly, forcing the eyes to close and flood with tears. In addition to coughing fits and difficulty in breathing, the targeted person is effectively blinded and incapacitated. Lachrymatory agents work on nerve receptors which help us sense heat and also induce an intense burning sensation. Tear gas is a weapon that disperses its contents, i.e, the irritants in the air either as liquid aerosol droplets (such as gas canisters), or as a powder (such as pepper balls) [6].

Figure 6 Pepper Spray

Figure 7 Tear Gas Canister

4.2 Dermal Patch

Neuropathic pain is a direct consequence of a disease affecting the somatosensory system or a lesion. Transient receptor potential vanilloid-1 (TRPV-1), a thermal nociceptor, plays an important role in the detection of painful stimuli such as heat, acids and irritant chemicals. Capsaicin is, highly selective TRPV-1 agonist. Capsaicin activates TRPV-1-expressing nociceptors on the skin, resulting in erythema. A high-concentration (8% w/w) capsaicin dermal patch (Qutenza®) has been developed which aims to provide long lasting pain relief following a single application. In the EU, the capsaicin 8% dermal patch is indicated for the treatment of PNP in adults, either alone or in combination with other medicinal products for pain [7].

Figure 8 Qutenza Ⓡ Patch

4.3 Clinical Uses

Capsaicin is being used for a number of diverse clinical conditions.

4.3.1 Chronic Pain Conditions

Capsaicin's main characteristic is specific binding to pain and heat receptors. Capsaicin used on the body causes a sensation of heat that activates certain nerve cells. This heating effect is reduced with Capsaicin application and the amount of substance P, a chemical that acts as a pain messenger in the body. Capsaicin is widely used as body ache ointments. Capsaicin is used in creams, gels and lotions to relieve muscle or joint pain and to provide temporary relief of muscle or joint pain caused by sprains, backaches, strains, bruising or arthritis. Capsaicin is used topically to treat various diseases such as rheumatoid arthritis, osteoarthritis, diabetic neuropathy, post therapeutic neuralgia, psoriasis and to reduce pain in Burning Mouth Syndrome, Guillain Barre syndrome, refractory pain, cluster headache, urticaria, rheumatoid arthritis and osteoarthritis, and atypical odontalgia [8].

Figure 9 Capsaicin Gel

4.3.2 Gastro Protection

The stomach receives a dense supply of TRPV1 bearing nerve fibres and these receptors are involved in gastric protection and inflammation. Capsaicin causes vasodilation and increased mucosal blood flow which is mediated by nitric oxide and CGRP released by these TRPV1 bearing cells. In a study on 84 young healthy adults, it was shown that capsaicin has protective properties against gastropathy associated with indomethacin and ethanol. Capsaicin increased the transmucosal potential difference in a dose-dependent manner. Gastric emptying was also increased. When Capsaicin is administered either before or after ethanol administration, it prevents the decrease in transmucosal potential difference induced by ethanol. The incidence of micro-bleeding associated with indomethacin administration was also reduced. The mucosal protective effect is mediated by the acute stimulatory effects causing mucosal hyperaemia rather than the desensitising effects of capsaicin [9].

4.3.3 Pruritus

Pruritus is common in patients receiving regular haemodialysis. It is suggested that substance P, which is depleted by capsaicin, is a mediator in the transmission of pruritus in renal failure. In a double – blind crossover study of 19 patients receiving regular haemodialysis, topical 0.025% capsaicin relieved the symptoms in 70% of patients compared with a placebo. Post-treatment, the antipruritic effect lasted up to 8 weeks. Pruritus is characterised by intense itching localised in the anus and perianal region and affects up to 5% of the population. In a prospective randomised crossover trial 31 of 44 patients experienced relief with a topical preparation of 0.006% capsaicin compared to menthol. [9]

4.3.4 Post – operative nausea, vomiting and sore throat

The efficacy of capsaicin applied at acupressure points prevents postoperative nausea and vomiting (PONV). In a randomised placebo – controlled trial of 186 patients undergoing laparoscopic cholecystectomy, 0.075% capsaicin ointment was applied at the K-D2 acupoint on the hand. The incidence of nausea was reduced at 6 h and at 24 h. In a study conducted on 160 patients undergoing abdominal hysterectomy, capsicum plaster was applied on either the K-D2 or P6 acupoints. This significantly reduced the incidence of vomiting (from 56% to 22%) and the need for rescue antiemetics compared to placebo.

Capsaicin also stimulates acupuncture points to reduce postoperative sore throat. In a trial on 150 patients undergoing abdominal hysterectomy, capsicum plaster was applied to the Korean hand acupuncture point (a point on the anterior aspect of the middle phalanx of the middle finger) for 8 h. Sore throat was significantly reduced. [9]

4.3.5 Myocardial ischaemia

A trial conducted on 12 patients showed that there was an increase in exercise time in patients with positive ischaemic stress tests when transdermal capsaicin patches were used. The levels of Nitric oxide increased in the blood and this suggested that NO mediated arterial and venous vasodilation was a possible mechanism to explain this clinical benefit. Calcitonin gene-related peptide (CGRP), a potent vasodilator which increases following capsaicin, however did not increase [9].

4.3.6 Overactive bladder and detrusor hyperactivity

Antimuscarinic drugs are used as a standard treatment for overactive bladders. Bladder capacity increases after intravesical application of capsaicin and resiniferatoxin. It also reduces the urge in patients with neurogenic and non-neurogenic detrusor hyper-reactivity. In hypersensitive bladder states, bladder pain is also reduced [9].

4.3.7 Cough and swallowing dysfunction

Silent aspiration caused by attenuation of cough reflex and swallowing reflex sensitivity is an important predisposing factor causing pneumonia in the elderly patients with stroke. A trial conducted on 64 elderly patients with cerebrovascular disease and swallowing and cough dysfunction, daily oral capsaicin supplements administered over 4 weeks. It was observed that the upper respiratory reflexes of the patients improved. It was also associated with an improvement in cough reflex sensitivity and a reduction in swallowing reflex latency time. This suggests that capsaicin may have therapeutic role to minimise aspiration pneumonia [9].

4.4 Anti – Cancer Properties of Capsaicin

Epidemiological and experimental evidence suggests that dietary phytochemicals such as Capsaicin have anticancer activity. Capsaicin strongly indicates significant anticancer benefits. Capsaicin alters the expression of several genes involved in growth arrest,cancer cell survival, metastasis and angiogenesis. Capsaicin induces apoptosis in many different types of cancer cell lines including pancreatic, colonic, prostatic, liver, esophageal, bladder, skin, leukemia, lung, and endothelial cells, while leaving normal cells unharmed. Capsaicin targets several proteins involved in the mitochondrial death pathway to initiate apoptosis in different cancer cell lines. Capsaicin was found to induce p53 phosphorylation at the Ser-15 residue and enhanced p53 acetylation through down-regulation of sirtuin 1, which is responsible for activation of apoptosis [10].

V. Conclusion

With a widespread application of capsaicinoids, nowadays people have started using it more and more. Many different techniques are being developed in order to reduce time and effort and increase the amount of capsaicinoids extracted from a chilli. Along with the current research going on in the field of capsaicinoids, more applications will be seen emerging [1].

References

[1] Stoica, R. M., Moscovici, M., Tomulescu, C., & Băbeanu, N. (2016). Extraction and analytical methods of capsaicinoids-a review. Sci Bull Ser F Biotechnol, 20, 93-8.

[2] Reyes-Escogido, M. D. L., Gonzalez-Mondragon, E. G., & Vazquez-Tzompantzi, E. (2011). Chemical and pharmacological aspects of capsaicin. Molecules, 16(2), 1253-1270.

[3] Werner, J. (2021). Capsaicinoids–Properties and Mechanisms of Pro-health Action. In Analytical Methods in the Determination of Bioactive Compounds and Elements in Food (pp. 193-225). Springer, Cham.

[4] Abdurahman, N. H., & Olalere, O. A. (2016). A Comparative Review of Con Extraction in Capsaicin Isolation Fr.

[5] Kaiser, M., Higuera, I., & Goycoolea, F. M. (2017). Capsaicinoids: occurrence, chemistry, biosynthesis, and biological effects. Fruit and Vegetable Phytochemicals: Chemistry and Human Health, 2nd Edition, 499-514.

[6] B. K. W. R. David Tidwell, Tear Gas and Pepper Spray Toxicity, 2021 Sep 22.

[7] H. A. Blair, Capsaicin 8% Dermal Patch: A Review in Peripheral Neuropathic Pain.

[8] A. B. P. D. J. S. a. K. M. C. K. Navaneetha, Formulation and In-Vitro Evaluation of Capsaicin Emulgel for Topical.

[9] P. C. K. Mark Hayman, Capsaicin: A review of its pharmacology and clinical applications.

[10] R. C. a. S.-H. LEE, Anticancer Properties of Capsaicin Against Human Cancer, Anticancer Research March 2016, 36 (3) 837-843.

Bibliography

[1] https://www.pepperscale.com/pepper-anatomy/

[2] https://science.thewire.in/the-sciences/pepper-spray-tear-gas-chemical-engineer-explains/