

Review of Capsaicin: an active ingredient of Capsicum

¹*Taif T. Surve, ¹Ruchika S. Batwal, ²Deeksha S. Chaskar, ³Sayali S. Pathak

^{*1}Student, Pharmaceutical Sciences, Sinhgad Institute of Pharmaceutical Sciences, Lonavala, Pune

^{2,3}Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Sinhgad Institute of Pharmaceutical Sciences, Pune

Date Of Submission: 01-04-2021

Date Of Acceptance: 14-04-2021

ABSTRACT: Capsicum annum (chili) is an important and common vegetable used in day-to-day life. It is the vegetable which is cultivated worldwide. It contains various active constituents which shows characteristic of capsicum. The medicinal properties of capsicum are popular for ayurvedic as well as for homeopathy treatment. This review is focused on Capsicum annum's active pharmaceutical component which is "capsaicin" and its morphology, history, natural function, mechanism of action, medicinal uses and research development.

I. INTRODUCTION:

Medicinal plants are the Nature's gift to human beings to help them pursue a disease-free healthy life, wide range of pharmacological effects were recorded to different medicinal plants. Genus capsicum is a member of family Solanaceae and have five species that are commonly recognized as domesticated: Capsicum annum, Capsicum baccatum, Capsicum chinense, Capsicum frutescens and capsicum pubescens.

Capsicum annum and capsicum frutescens were widely distributed from the new world to other continents via Spanish and Portuguese traders while the other species are little distributed outside South America. Only two species C. annum and C. frutescens were grown in Iraq. Shape and colour variation of C. annum is similar with C. frutescens.

Capsicum (Capsicum annum), also known as cayenne pepper, has been used orally for upset stomach, poor circulation, fever,

hyperlipidemia and heart disease prevention. Capsicum can be used topically to treat pain associated with osteoarthritis, rheumatoid arthritis, post-herpetic neuralgia, trigeminal neuralgia, diabetic neuropathy, fibromyalgia and back pain. Capsicum can also be used as gargle for laryngitis and for relief of muscle spasms.

It contains varieties of carotenoids, including capsanthin, capsorubin, beta-carotene, lutein, phytofluene, and xanthophyll and steroids including capsicoside. One of the main constituent is capsaicin (methyl-n-vanillyl noneamide), which produces an intense burning sensation when it comes into contact with the skin, eyes or mucous membrane and which gives peppers their burning taste.

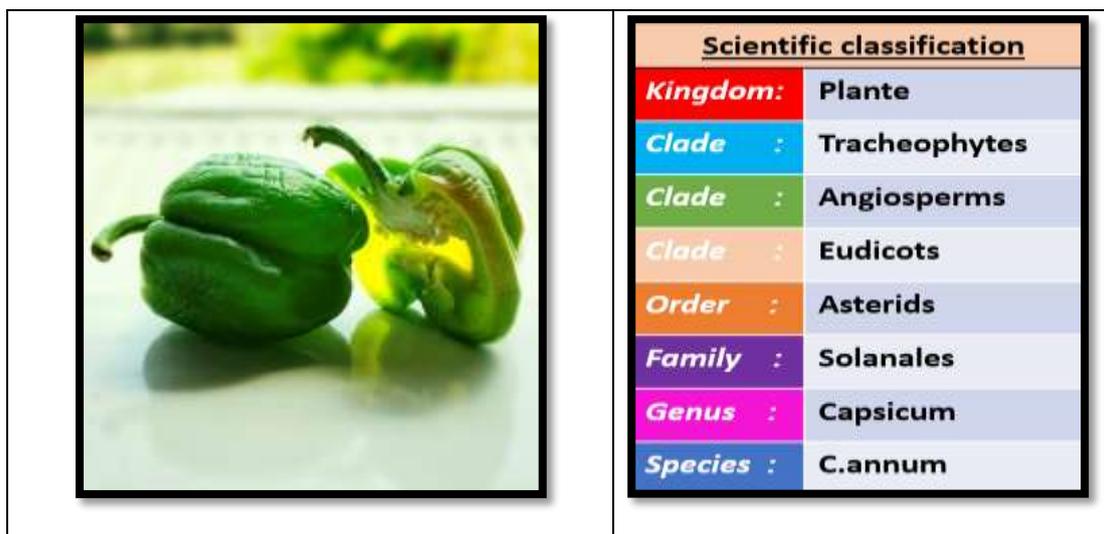
Capsicum annum and Capsicum frutescens species contained a wide range of nutritional components and pharmacologically active metabolites. They supply good level of antioxidant and vitamin C. Both species exerted a wide range of pharmacological activities. The present review will highlight the chemical constituents and the pharmacological and therapeutic effects of capsicum annum

There are different varieties and group of capsicum annum, some of them are:

- C. annum var. annum
- C. annum var. glabriusculum
- Capsicum annum var. bola (aka var. ñora)
- Capsicum annum 'New Mexico Group'

Table No.1

Photograph of Capsicum	Details of capsicum



Morphological features of capsicum :

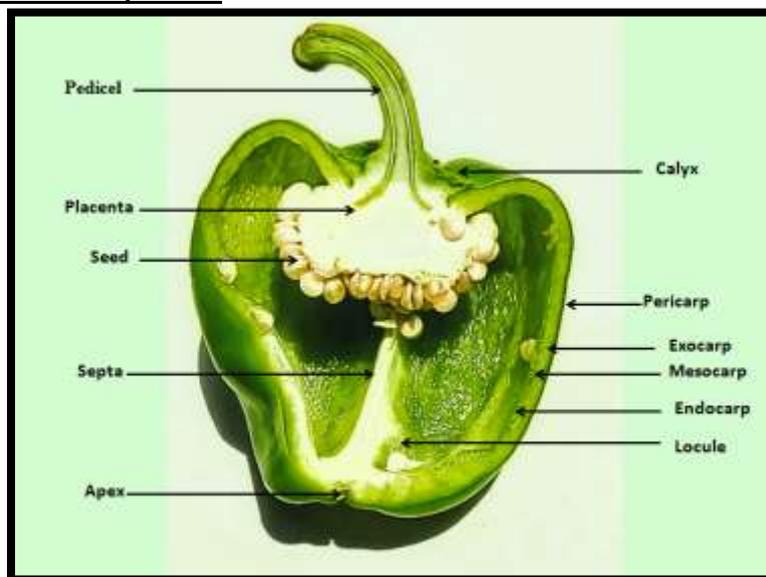


Figure No. 1

Pedicel: a little more or less long branch which ends the flower.

Calyx: It is the structural base of the flower which is generally green in colour

Placenta: It is the region where the seeds are attached.

Seeds: The seeds are campylotropus, ellipsoid, long and broad, oval in longitudinal section.

Pericarp: Contains many seeds embedded in a solid mass, it is composed of three clearly distinct

areas differently which are Exocarp, Mesocarp and endocarp.

Exocarp: It has uniseriate and smooth epidermis with no overlapping tubular cells and it has dense textured and cellulosic wall.

Mesocarp: composed of five collenchyma layers followed by the parenchyma and vascular bundles accompanied by external fibres.

Endocarp: It is uniseriate and lacked stomata. It is composed of parenchyma cells with different size and shapes within the wall

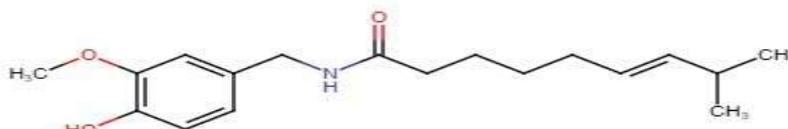
Septa: It is a wall which divides the fruit into smaller cavity

Apex: It is the terminal portion of fruit.[3]

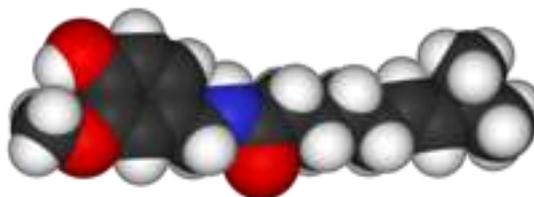
Active pharmaceutical component in Capsicum:

- **Capsaicin (8-methyl-N-vanillyl-6-nonenamide)** is an active component of chili peppers, which are plants belonging to the genus Capsicum.
- It is a chemical irritant for mammals, including humans, and produces a sensation of burning in any tissue with which it comes into contact.

- Capsaicin and several related alkaloids are called **Capsaicinoids** and are produced as secondary metabolites by chili peppers, probably as deterrents against certain mammals and fungi.
- Pure Capsaicin is a hydrophobic, colorless, highly pungent, crystalline to waxy solid compound.[4]
- It is the most commonly occurring Capsaicinoids(69%).
- Its **Scoville heat unit** is 16,000,000.[5]



CAPSAICIN



(3D STRUCTURE OF CAPSAICIN)

Properties:

- ✓ Chemical formula- C₁₈H₂₇NO₃
- ✓ Molar mass- 305.418g.mol⁻¹
- ✓ Appearance- Crystalline white powder
- ✓ Odor- Highly volatile and pungent
- ✓ Melting point- 62 to 65°C (144 to 149 °F; 335 to 338 K)
- ✓ Boiling point- 210 to 22 °C (410 to 428°F; 483 to 493 K)
- ✓ Solubility in water- 0.0013 g/ 100 ml
- ✓ Solubility- Soluble in alcohol, ether, benzene
- Slightly soluble in CS₂, HCL, Petroleum.
- ✓ Vapor pressure- 1.32x10⁻⁸mm Hg at 25°C.[6]

Biosynthesis of capsaicin:

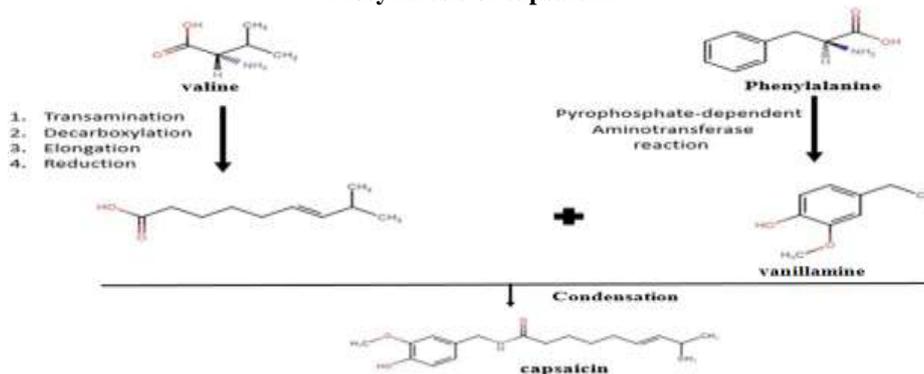


Figure No. 2

History of Capsaicin:

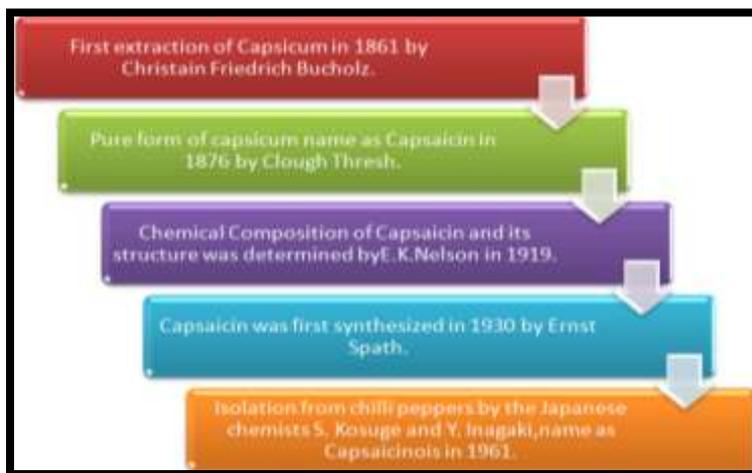


Figure No. 3

Natural Function:

- Capsaicin is present in large quantities in the placental tissue(which holds the seed), the internal membranes and, to a lesser extent, the other fleshy parts of the fruits of plants in the genus Capsicum. The seeds themselves do not produce any capsaicin, although the highest concentration of capsaicin can be found in the white pith of inner wall, where the seeds are attached.
- The seeds of capsicum plants are dispersed predominantly by birds. In birds, the TRPV1 channel does not respond to capsaicin or related chemical.

- This is advantageous to the plant, as chili pepper seeds consumed by birds pass through the digestive tract and can germinate later, where as mammals have molar teeth which destroy such seeds and prevent them from germinating. Thus, natural selection may have led to increasing capsaicin production because it makes the plant less likely to be eaten by animals that do not help it disperse.
- Capsaicin may have evolved as an anti-fungal agent. The fungal pathogen Fusarium, which is known to infect wild chilies and thereby reduce seed viability, is deterred by capsaicin, which thus limits this form of predispersal seed mortality.[14]

Mechanisms of Action of Capsaicin:

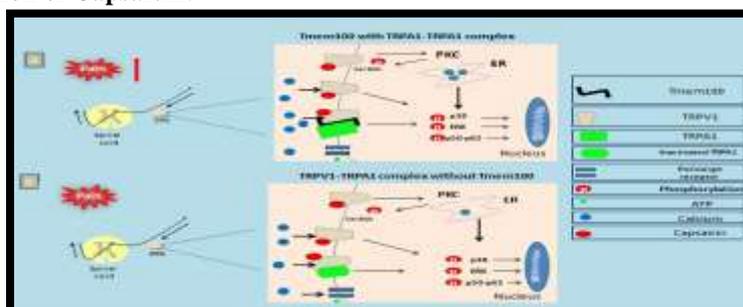


Figure No. 4

(Mechanisms of capsaicin- induced pain. Schematic representation of the Phosphorylation at ser800, which allows TRPV1 (The transient receptor potential cation channel subfamily V

member 1) discriminating cation influx, and participation of Tmem100 in the mechanism of capsaicin-induced pain.)

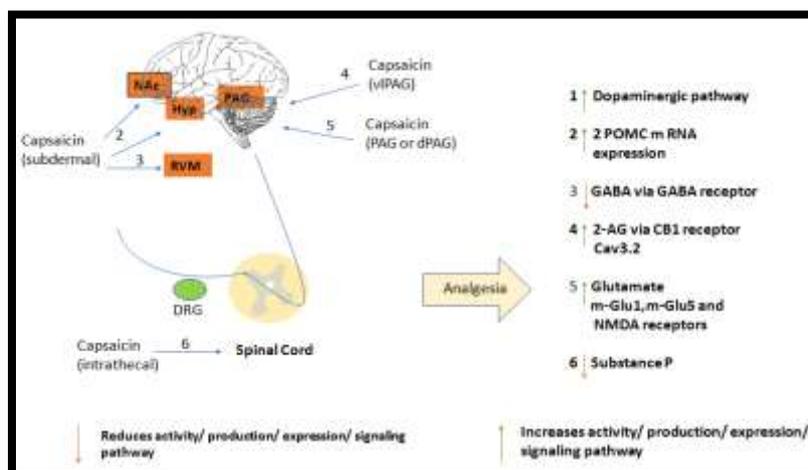


Figure No. 5

(Supraspinal mechanisms of capsaicin-induced analgesia. Subdermal injection of capsaicin produces analgesia by modulating dopaminergic pathway in the NAc, opioid pathway in the hippocampus, and GABAergic activity in the RVM.) [15]

Research and Pharmaceutical use:

- Capsaicin is used as an analgesic in topical ointments and dermal patches to relieve pain, typically in concentration between 0.25% and 0.1%. It may be applied in cream form for the temporary relief of minor aches and pains of muscles and joints associated with arthritis.
- It is also used to reduce the symptoms of peripheral neuropathy, such as Post-herpetic neuralgia caused by shingles.
- Although capsaicin creams have been used to treat psoriasis for reduction of itching. Clinical trials involving topical capsaicin for treatment of pruritus concluded there was insufficient evidence of effect.

There is insufficient clinical evidence to determine the role of ingested capsaicin on several human disorders, including obesity, diabetes, cancer and cardiovascular diseases.

- Because of the burning sensation caused by capsaicin when it comes in contact with mucous membranes, it is commonly used in food products to provide added spice or heat (piquancy), usually in the form of spices such as chili powder and paprika.

- In high concentrations, capsaicin will also cause a burning effect on other sensitive areas, such as skin or eyes.
- The degree of heat found within a food is often measured on the Scoville scale. Because some people enjoy the heat, there has long been a demand for capsaicin-spiced products like chili pepper, and hot sauces such as Tabasco sauce and salsa.
- Folklore among self-described ‘chiliheads’ attributes this to pain-stimulated release of endorphins, a different mechanism from the local receptor overload that makes capsaicin effective as a topical analgesic.

Equestrian sports:

Capsaicin is a banned substance in equestrian sports because of its hypersensitizing and pain-relieving properties. At the show jumping events of 2008 summer Olympics, four horses tested positive for the substance, which resulted in disqualification.

MEDICINAL PROFILE OF CAPSICUM ANNUM:

- In addition to the use of capsicum fruits as a food additive, in traditional medicine, it has been used for the treatment of cough, toothache, sore, throat, parasitic infections, rheumatism, wound healing and also utilized as an antiseptic, appetite stimulator, antioxidant and immunomodulator.
- Other effects such as antibacterial and anticancer are also related to chilies. Red pepper as a drug is given in atonic dyspepsia

and flatulence due to increasing the motility in the gastric antrum, duodenum, proximal jejunum and colon.

- It can also increase parietal, pepsin, and bile acid secretions. Chilies are known to protect against gastrointestinal ailments including

dyspepsia, loss of appetite, gastroesophageal reflux disease and gastric ulcer due to the several mechanisms such as reducing the food transition time through the gastrointestinal tract and anti-*Helico pylori* effects. Moreover, the leaves of its plant have antioxidant activity.

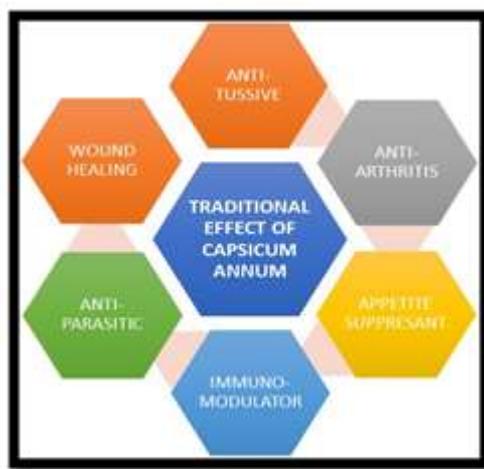


Figure No. 6

The medicinal effects of chilies are related to different constituents such as capsaicin, fixed oil, thiamine, protein and ascorbic acid.

- Capsaicin, water-insoluble derivative of homovanillic acid and the main active ingredient in capsicum fruits, is responsible for hot sensation to the tongue and is utilized for the treatment of inflammatory disorders such as psoriasis and rheumatoid arthritis, diabetic neuropath, postherpetic neuralgia, cluster headache, dermatitis or eczema itching, bladder hyperactivity, liver congestion, oodborne gastrointestinal pathogens including *Listeria monocytogenes*, *salmonella typhimurium* and fibromyalgia.
- It is also used as pesticides analgesic, antiobesity, antihypertensive, antiarrhythmic, antiischemic and gastroprotective agent.
- It can stimulate saliva and digestive enzymes of the pancreas, small intestine and also stimulate hair growth in alopecia areata.
- Anticoagulant activity, prevention of aspiration pneumonia, protecting neuromuscular junctions from *Clostridium botulinum* neurotoxin A and improving cognitive function are also attributed to capsaicin beneficial properties..

Different studies indicated that capsicum and its active constituent, capsaicin, have therapeutic potential in different components of metabolic syndrome.

Effect on Hyperglycemia:

Diabetes, which is correlated with some problems, including hypertension, atherosclerosis and microcirculatory disorders, increases morbidity and mortality. Type 2 diabetic patients are insulin resistance and most of them have metabolic syndrome. *C. annum* has been shown to have an antidiabetic effect via several mechanisms including inhibition of α -amylase and α -glucosidase activity (enzymes which can hydrolyze polysaccharides into glucose), antioxidant activity, insulin mimetic or secretagogues, weight regulation and hypolipidemic effects of this plant, activation of transient receptor potential vanilloid subtype 1 (TRPV1).

Which leads to the improvement of insulin resistance, suppress inflammation, glucose homeostasis regulation, increasing insulin sensitivity in peripheral tissues, stimulation of glucagon-like peptide-1 (GLP1) Secretion, improvement in glucose/ insulin level as well as expression of adipocytokine genes.

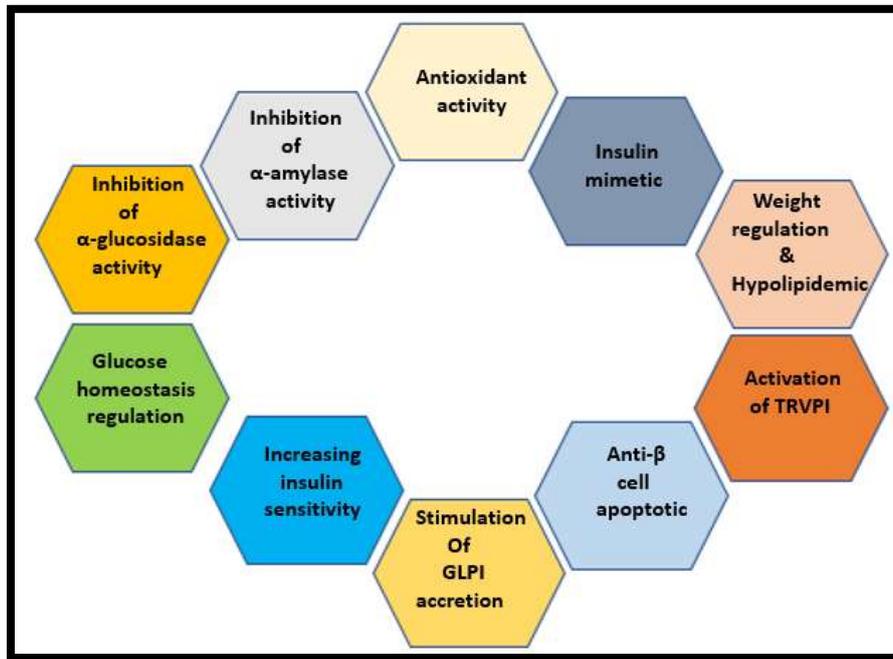


Figure No 7

(Mechanisms of Capsicum annum antidiabetic effects GLP1: glucagon-like peptide-1; TRPV1: transient receptor potential vanilloid subtype 1)

Effect on High Blood Pressure:

One of the main risk factors for CVD is hypertension which is referred to the instability between vasodilation and vasoconstriction. Red pepper and its constituent, capsaicin, exerted their antihypertensive effect by several mechanisms, including releasing vasodilator neuropeptides through TRPV1 activation, stimulating of natriuresis and diuresis, an angiotensin-converting-enzyme(ACE) Inhibitory activity and L-type Ca²⁺ channel inhibition in smooth muscle cells.

Effect on Obesity:

Red chili pepper exhibited anti-obesity effect by different mechanisms including Thermogenesis, satiety, fat oxidation, elevation of energy expenditure, reduction of energy intake, prevention of adipogenesis, restriction the activity of lipoprotein lipase and pancreatic lipase, stimulation of lipolysis in adipose tissue and modulating adipokine release from adipose tissues.

For examples, in animal studies, capsaicin exhibited antiobesity effects via inhibitionof the generation white fat cells and restricted the activity of lipoprotein lipase.

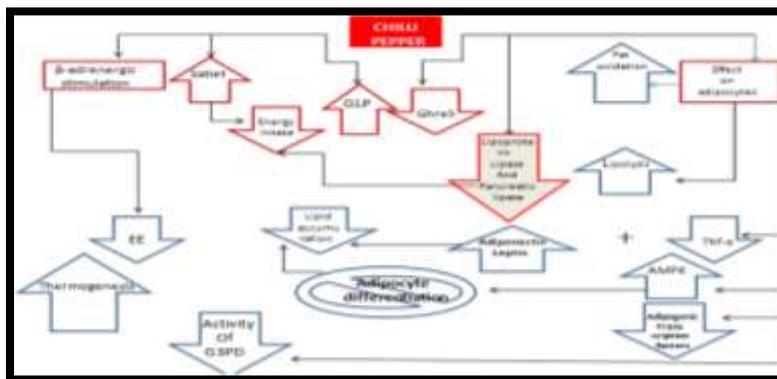


Figure No. 8 (Mechanism of capsicum annum and capsaicin anti-diabetic effects.)

Clinically Available Capsaicin Pharmaceutical Formulations:

- Oral administration of capsaicin are available in the form of capsules containing chili paper.
- The generally recommended daily dose of oral administration is 1350-4000 mg of capsicum with 0.25% capsaicin.
- This range of dose has been shown to increase energy expenditure, fat oxidation, Thermogenesis, and decrease appetite in humans.
- Other Pharmaceutical formulations containing capsaicin are capsicum nasal sprays and homeopathic preparation of capsicum annuum and Eucalyptol nasal sprays.
- These formulations have been used to treat nonallergic rhinitis and the symptoms associated with this condition.
- E.g.:- walgreens arthritis pain relief capsaicin 0.1% / Topical analgesic cream; XLEAR MAX natural saline sinus spray with capsicum .[15]

II. CONCLUSION AND FUTURE PERSPECTIVE OF CAPSICUM ANNUUM:

As in upper study we come to know that capsaicin which is the active pharmaceutical ingredient of capsicum have many beneficial uses, in medicinal profile we studied that it is used for treating many medical conditions such as obesity, cancer, arthritis and many more. Capsaicin is essential to our understanding of physiological action processes as well as their relevance of TRPV1 channel. Capsaicin's importance is confirmed by various available pharmaceutical formulations. Advanced SAR studies are needed to be designed for the identification of capsaicin analogues with less or no toxic effect. Despite being an old molecule capsaicin is still a hot topic in scientific community and it has wide potential in future for therapeutic uses.

REFERENCE:

- [1]. Al-Snafi, Ali. (2015). "The pharmacological importance of capsicum species (capsicum annuum and capsicum frutescent) grown in Iraq." *Journal of pharmaceutical biology*, 5(3), pp 124-142.
- [2]. Nelson EK, (1919). "The constitution of capsaicin, the pungent principle of capsicum" *Journal of American Chemical Society* 41 (7): pp 1115–1121.
- [3]. Howard L., Geoffrey A., Cordell P., (1996). "Nonivamide, a Constituent of Capsicum oleoresin". *Journal of Natural Products*. 59 (4): 425–426.
- [4]. Nelson EK (1919). "The constitution of capsaicin, the pungent principle of capsicum" *Journal of American Chemical Society* 41 (7): pp 1115–1121.
- [5]. Nllis CN, Berberian B,(1993). "A double-blind evaluation of topical capsaicin in pruritic psoriasis". *Journal of American academy of dermatology*. 29(3) ; pp 438-42
- [6]. Gooding SM, Canter PH, Coelho HF(2010). "Systematic review of topical capsaicin in the treatment of pruritus". *International journal of dermatology*; 49(8): pp 858-65.
- [7]. [24] Satareh Sanati¹, Bibi Marjan Razavi² (2018 May). A review of the effects of Capsicum annuum L. and its constituent, in medical syndrome. *Iranian journal of medical sciences*;21(5);pp 439-48
- [8]. Glinski W, Glinska-Ferenz M, Pierzynska-Dubowska M (1991). "Neurological inflammation induced by capsaicin in patient with psoriasis". *Acta dermato.Venereologica*.;71 (1) ;pp 51-4.