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A SCIENTIFIC REVIEW REGARDING HEALTH BENEFITS OF CHILLIES

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Abstract: Chillies are among the most well-known plant spices in the world. Originating from the South American continent, nowadays it is wildly spread in the culinary world, but it makes a great subject for medical research also. Chillies are part of the genus *Capsicum*, within the *Solanaceae* family, which includes approximately thirty-seven wild and five domesticated species: *C. annum*, *C. frutescens*, *C. baccatum*, *C. chinense*, *and C. pubescens.* Chillies and fermented chilli sauces differentiate mainly by pungency, which is due to the different content in specific alkaloids, commonly known as capsaicinoids. Peppers represent a good source of carotenoidic pigments which include β-carotene, lycopene, lutein, zeaxanthyn and two main compounds specific to pepper fruits: capsanthin and capsorubin. Beside these compounds, peppers are rich in vitamin C, phenols, tocopherols and other biologically active compounds. Fermented and unfermented chilli is also studied for its potential health benefits (anti-tumoral, anti-diabetic, etc.), whereas capsaicin in particular is considered to have antimicrobial/antifungal properties.

***Keywords*:** chilli, fermented chilli, capsaicin, biomolecules, antimicrobial activity

Introduction and botanical origins

The genus Capsicum includes five domesticated species spread unevenly across the globe: *C. annum*, *C. frutescens*, *C. baccatum*, *C. chinense*, *and C. pubescens. C. chinense* includes cultivars with high capsaicin content and is mostly cultivated in South America, whereas *C. frutescens* is becoming more popular in Asia and Africa. *C. pubescens* and *C.baccatum* can rarely be found outside Latin America and the Andes (Guillen, 2018). Under temperate climate, pepper plants become annual, although in tropical regions they are perennials. *C. annuum*, *C. chinense* and *C. frutescens* are phylogenetically related, common patterns can be seen in their white-greenish petals and yellow seeds (Hassan, 2019). Peppers develop small seeds

with an average weight of 5-7g/1000 units, with a germinating capacity up to 3-4 years. Plants are generally self-pollinators although cross-pollination can sometimes occur. Characteristics of the fruit (colour, shape, pungency, etc.) differentiate by endogenic (cultivars) (Figure 1) and exogenic factors (soil, climate, moisture, drought, etc.). Growth of chilli plants can be continuous or determinate.

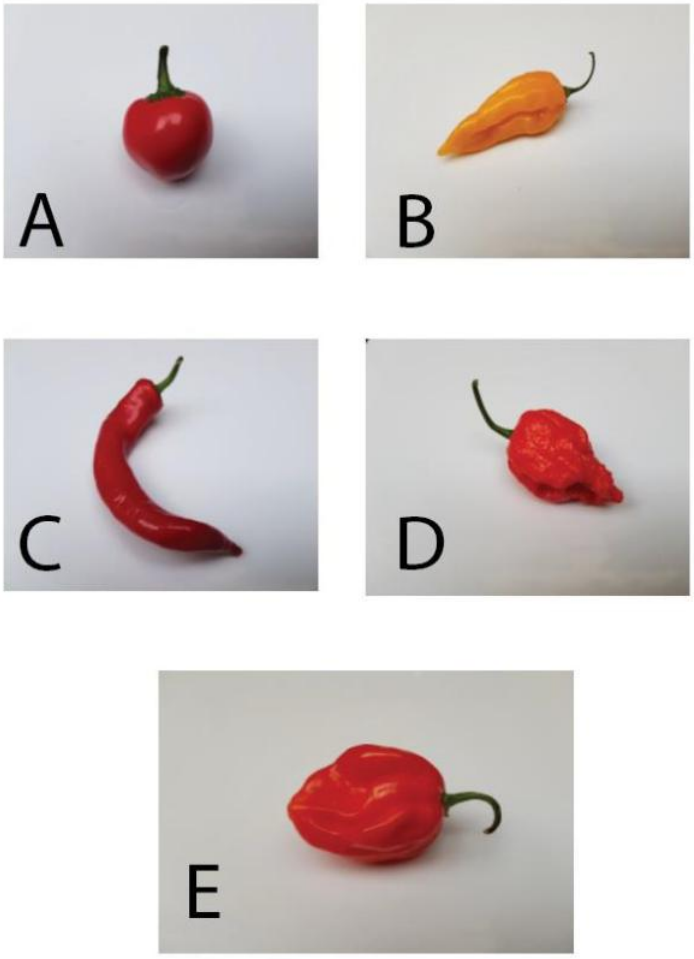

Figure 1. Fruits of different chilli cultivars:
A (Cherry), B (Fatalii), C (Cayenne), D (Carolina Reaper), E (Habanero Red)

Roots of the plant penetrate approximately 30 cm beneath the topsoil, development of the roots being mainly horizontal. Leaves usually present a lanceolate form with different colours across varieties. Some cultivars can present a hair like coverage on their leaves, ex. 'Serrano' (Nagy, 2018).

Chilli has its origin from Latin America, and it was discovered during the expeditions of Columbus in the late 14th century, being introduced in Europe in 1494. Since then it became a highly cultivated crop mainly in different regions of Turkey and Spain. In South America, wild species are cultivated primarily in Brazil, whereas domesticated species are spread in Mexico, Bolivia and Peru.

Capsaicinoids and pungency

Capsaicin and its derivatives are the main compounds responsible for the pungent taste of chilli peppers (Wenjing, 2019). Chemically they are very stable alkaloids synthesized exclusively in chillies. Biosynthesis of capsaicinoids involves two main steps: the phenylpropanoidic pathway, involving the formation of vanillylamine from phenylalanine and the formation of 8-Methyl-6-nonenoic-S-CoA from Valine. Condensation of the formed components is catalysed by an acyltransferaze. This reaction represents the final step in capsaicin synthesis. The reactions take place exclusively in the placenta of chilli fruits in about 20-30 days after flowering. Other parts of the fruit (seeds) can uptake minor concentrations of capsaicin threw absorption (Bosland, 1996), leading to uneven distribution of the molecules in the fruit. Capsaicin and dihidrocapsaicin can add up approximately 80% of the total capsaicinoids (Guillen, 2018).

In an attempt to differentiate chillies by their pungency, the Scoville test was developed in the 19th century. This test is based on the successive dilution and tasting of samples until pungency becomes unperceivable. Results are counted as heat units. *C. chinense* includes cultivars with high amount of capsaicin ('Habanero'); cultivars in this category can reach up to 500.000-1.000.000 SHU. Modern techniques require the analysis of methanolic (or other solvent) extracts of the samples by HPLC. These methods are highly reliable and can give accurate measurements.

Biosynthesis of capsaicin can be genetically traced back to a gene named *Pun1*. This gene codifies an enzyme called acyltransferase that is needed in the last phase of the synthesis, regarding the condensation of vanillylamine and 8-Methyl-6-nonenoic-S-CoA. It has been shown that sweet varieties of pepper contain high amounts of vanillylamine. This leads to the presumption that the absence of the mentioned acyltransferase prevents the last step required for capsaicin formation (Ogawa, 2015). This example can highlight the importance of each step in the reaction chains, and how such minor steps can affect results.

Different studies highlight the influence of stressing factors on capsaicinoids accumulation. It has been shown that plant stressing conditions

can increase capsaicinoids accumulation. Drought and high temperatures make chillies more pungent. This might explain why Mexican chillies and chilli products are considered of better quality.

Carotenoids and colour

Chillies are amongst the most diversely coloured fruits, pallets can reach from green up to different shades of brown, yellow or red. Responsible for this vast spectrum of colours are a group of pigments called generically carotenoids. Carotenoids represent a group of biomolecules with cyclical or aliphatic structure, manifesting strong antioxidant activity, and having a protective role against free radicals, formed in oxidative phosphorylation.

Colour changes in the pericarp of chillies occur through complex reactions catalysed by different enzymes (El-Sayed, 2013). In the first phase, when the fruit is still green, the main pigment in the pericarp is chlorophyll (68%), whereas carotenoids represent fewer than 32%. As the fruits start to ripen, the percentage changes in favour of yellow and red pigments (Figure 2) whereas in the last phase two specific compounds occur, synthesized exclusively in peppers: capsanthyn-3-6-epoxide and capsorubin (Hassan, 2019). Amongst more than 600 carotenoids known, more than 20 can be identified in pepper fruits. Yellow varieties may lack certain enzymes, or these might be deactivated during ripening. For example, in the absence of capsanthin-capsorubin synthase, red pigment formation is blocked, meaning that the final colour of the fruit will be yellow or orange. In this case capsanthin and capsorubin precursors (ex. violaxanthin) will be the main pigment, giving the fruit its specific colour.

green pigments	Chlorophyll
yellow and orange pigments	B-Carotene
	Lutein
	Zeaxanthin
	Violaxanthin
red pigments	Antheraxanthin
	Capsanthin
	Capsorubin
	Capsanthin-3,6-epoxide

Figure 2. Specific pigments and colour variation in chillies: colour of peppers is given by the dominant pigment in different stages of maturity
(Adapted after Hassan, 2019)

Health benefits of chilli consumption

Chilli consumption is associated with many health benefits. These benefits can be traced back to biologically active compounds, such as vitamin C, capsaicinoids, carotenoids, phenolic compounds, etc.

Laboratory analysis shows that peppers in general contain high amounts of ascorbic acid. Values can fluctuate between 128-183mg/100g depending on many factors. Vitamin C is involved in many biological processes, being extremely important in wound healings and collagen synthesis (Fain, 2004). It also plays an important role as free radical scavenger, whereas it can also decrease recovery of the body after certain illnesses.

Some studies suggest that capsaicin can behave as an anti-lipogenic compound in HepG2 cells, meaning that it might help fighting obesity (Bort, 2019). Other findings show a possible inhibitory effect against alpha-glucosidase, alpha-amylase sand tyrosinase (Nanok, 2020). Results suggest the possibility of the utilization of capsaicin and dihydrocapsaicin for drug developments in the pharmaceutical and cosmetic industry.

Carotenoids are powerful antioxidants due to their extended linear system of conjugated double bonds which allows resonance to occur and maintain the stability of the molecule. Antioxidant activity of pepper fruits increase with advancement of ripening (Conforti, 2006). In a study conducted on antioxidant activity of pepper extract, in different maturity stages indicated that the highest antioxidant activity can be shown in mature, red fruits when pigments are the most concentrated (Conforti, 2006). Fractions from mature and immature Habanero peppers showed good inhibitory effect against α-amylase. The inhibitory effect on hydrolysing enzymes lengthens carbohydrate digestion time, exerting a positive effect on glucose absorption.

Chilli fermentation and fermented chilli products

Fermented hot sauces are one of the main products obtained from different peppers and chilli cultivars. Hot sauces are generally obtained under spontaneous fermentation, initiated by soil specific microorganisms (Wang, 2019) under anaerobic conditions. Products can be fermented whole in brines prepared with 2.5% salt and blended afterwards or they can be blended first and fermented after (Koh, 2005).

Fermentation is usually initiated by *Leuconostoc mesenteroides*. These bacteria create specific conditions required afterwards for the development of *Lactobacillus plantarum* (Raghuvanshi, 2019). *L. mesenteroides* multiplies in the first 2-3 days. This phase is characterized by the rapid downfall of pH, metabolism of carbohydrates and the rapid consumption of O_2 in the brine.

Acidity can reach values near 4 in the first 3-4 days leading to specific conditions required by lactobacilli and putting a bourdon on the metabolism of pathogens (Koh, 2005). After the first few days *Leuconostoc* cells drop in numbers, domination being overtaken by *L. plantarum*. These microorganisms are anaerobes with some kind of toleration for oxygen. This leads to certain conditions that need to be fulfilled in vegetable fermentation: perfect sealing of barrels, high acidity in the brine, etc.

Fermenting processes imply complex transformations of raw materials, elimination of certain molecules and transformation of others. Sugars are being metabolized thus leading to the formation of lactic acid, vitamin C stabilizes by oxygen elimination from the system, and other vitamins are synthesized, aromatic compound form and are released in the brine (Hamed, 2019).

Interestingly data regarding correlations between lactic acid bacteria and capsaicin concentration could not be found, leading to possible future studies regarding the impact of capsaicin on fermentation processes.

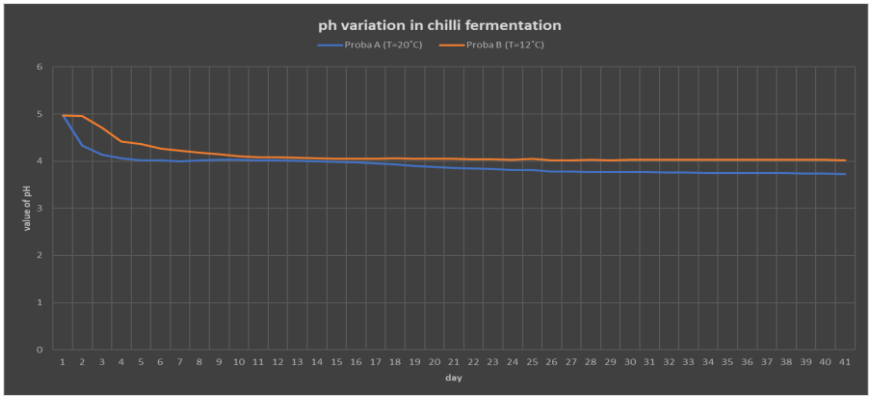

Figure 3. pH variation over a 41-day period in chilly fermentation at different temperatures

Chilli pastes or chilli sauces are fermented according to the desires for the final product, lasting between a couple of days and up to 1-2 years. After fermentation and blending, final products are generally pasteurized and acetic acid is added for further drop of pH. Perfect stability occurs at values below 3.5 (Lobo, 2019).

Commercial sauces are usually mixed with other materials such as corn syrup, additives and other substances that enhance flavour. This leads on one hand to the loss of potential probiotics and vitamins (partially) and overbalancing the biological quality of the sauce by adding refined sugars and additives on the other. Although chilli sauces are being studied for positive

health effects, elimination of over processing should be reconsidered for the true enhancement of its beneficial effects.

A study was conducted regarding consumer preferences for chilli sauces (Kim, 2018). The results of the study reveal that sweet sauces with low pungency are rejected by American consumers, whereas Koreans dislike pungent sauces insufficiently sweetened. Some studies indicate a positive correlation between chilli consumption and positive health issues. It was noted that people consuming chillies and chilli sauces on a general basis have lower mortality rates, smaller percentages in coronary and heart disease issues and they might be better protected against cancer (Hamed, 2019).

Antimicrobial and antifungal activity of chillies and fermented hot sauces

It is universally recognized that plants contain molecules that can exert more or less effective antimicrobial and/or antifungal activity (Adams, 2020). This is usually correlated with certain bio-molecules specific to different parts of different plants. Some plants, like thyme, mint, oregano, etc., or other aromatic plants contain volatile oils, phenolic compounds and other molecules that can exert (individual or synergetic) antimicrobial/antifungal activity. These molecules although not as powerful as synthetic antibacterial substances, they might be the solution against pathogens in an era with everlasting antibacterial resistance (adaptation). Resistance against natural antibiotics is not heard of and studies suggest real potential in this field.

Bacon (2016) conducted a study to explore chilli fractions that present antimicrobial activity. Amongst many fractions there was only one that clearly presented antimicrobial activity against *L. monocytogenes*. After subjection to further HPLC-MS analysis, it has been shown that the studied fraction contained capsaicin-like compounds. Bacon suggested that further experiments should be done in order to fully confirm that capsaicin is the main antimicrobial compound. At the time of the experiments pure capsaicin was not available as standard.

Another research was conducted by Das *et al.* (2018) regarding antimicrobial activity of acetonitrile extract of two *C. chinense* varieties: Roja Bhut and Noga Bhut. Results indicate that concentrations higher than 25% extract showed inhibition (8-9 mm) against *E. coli* and *S. aureus* in the disk diffusion test. Inhibition increased proportionally with the concentration of the extract. Taking into account the types of microorganisms the study has been conducted on, the results are quite interesting. However, these varieties of chillies are amongst the hottest, meaning that antimicrobial activity of capsaicin may appear at concentrations far over the limits of usual consumption.

Table 1.
Antimicrobial activity of acetonitrile extracts of *C. chinense* var. 'Roja Bhut' and *C. chinense* var. 'Noga Bhut' using the disk diffusion assay

Chili extract (acetonitrile)	*Staphylococcus aureus*	*Escherichia coli*
	Zone of inhibition (mm)	Zone of inhibition (mm)
'Noga Bhut'		
10%	No zone	No zone
25%	9	8
50%	10	9
75%	11	10
Positive control	17	17
Negative control	No zone	No zone
'Roja Bhut'		
10%	No zone	No zone
25%	8	9
50%	9	10
75%	10	12
Positive control	17	17
Negative control	No zone	No zone

(Adapted after Das *et al*., 2018)

Marini (2015) studied the dynamics of virulent and non-virulent *S. pyogenes* exposed to different concentrations of capsaicin by the microdilution test. The minimum inhibitory effect against the pathogen was determined at 128μg/ml. Interestingly, sub-lethal doses of capsaicin induced biofilm production and a drastic reduction in virulence. These results indicate that capsaicin could prevent formation of intracellular reservoir and spreading of infections.

It has been shown that pathogens like *E. coli* can only be retarded at concentrations between 200-300 μg/ml (Omolo *et al*., 2014). However, 10 μg/ml of capsaicin successfully inhibits *Helicobacter pylori* (Jones, 1997) with a maximum effect at concentrations of 50 μg/ml. Decreasing pH values also alleviates antibacterial effect of capsaicin. In the case of *V. cholerae* it was determined that capsaicin extract acts more likely against virulence expression rather than viability.

Conclusions

Threw the vast fields of nature and biodiversity, chillies might represent a small niche, although on many occasions a single species may reflect a huge diversity. Studies regarding chillies are based on possible health-benefits that might be attributed to biomolecules extracted from different parts of the plant.

As we have seen it before, many correlations have been made between consumption of chilli fruits and certain health benefits. Medical sciences focus on targeted molecules, like capsaicin for specific actions: anti-microbial, anti-diabetic, anti-tumoral, etc. Although many secrets have been revealed since the beginning, there are still much more facts to be discovered. For each molecule that is being characterized, there are thousands that are not properly studied or understood. Therefor research is needed to be done for further examination of capsaicin and other compounds within the *Solanaceae* family. Future studies might reveal correlations between capsaicin and fermentation processes, chillies and gut microbiota, possible uses as food preservatives and many more.

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