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Article Review

Bioactive Compounds Content and Pharmacological Activities of Chili Pepper (*Capsicum* Sp.)

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ABSTRACT

Chili pepper (*Capsicum* sp.) is an essential spice belonging to the Solanaceae family. Chili pepper is consumed as a food source, additive in the food industry, and necessary medicine. Chili pepper is rich in nutrients and secondary metabolites to generate new bioactive compounds. Chili pepper fruit contains bioactive compounds including alkaloids, capsaicinoid, carotenoids (anteraxanthin, β-carotene, capsanthin, violaxanthin, β-cryptoxanthin, zeaxanthin, lutein epoxide, capsorubin, and neoxanthin), peptides (defensin, thionin-like peptide), phytol, fatty acids (myristic acid, methyl stearic, methyl linoleic), phenolic (chlorogenic acid) and flavonoids (quercetin, luteolin, rutin). The compounds in chili pepper constitute a bioactive source that acts as an antioxidant, antimicrobial, antifungal, anti-inflammatory, anti-obesity, anti-diabetic, and dyslipidemia. This review intends to describe the content of bioactive compounds that are very beneficial for health. This review is expected to increase chili consumption and its application in the food industry

1. INTRODUCTION

The genus *Capsicum* is known by several universal names in English, including hot pepper, chili pepper, chili, sweet pepper, and bell pepper, which are members of the Solanaceae family. Chili pepper consists of about 27 species, and five are widely cultivated. Chili pepper is an important vegetable and a popular spice grown in tropical and subtropical regions (Olatunji et al., 2019). *Capsicum* is characterized by vitamin C, vitamin A, high mineral content, and antioxidant compounds, including carotenoids, flavonoids, and polyphenols (Palma et al., 2020). Chili pepper is consumed worldwide, an important spice and the most widely consumed as food. Chili pepper is also used as an additive in the food industry and has an essential role in medicine (Hernandez-Ortega et al., 2012).

Capsicum is a source of capsaicinoids, carotenoids (provitamin A), flavonoids, essential oils, ascorbic acid (vitamin C), and tocopherols (vitamin E). Antifungal, antibacterial, and mineral compounds are also found in chili peppers (Sarpras et al., 2019). The biochemical components in chili pepper are valuable for the plant itself and the health of other living things. The antioxidant activity of polyphenolic compounds can reduce free radicals, have the potential as anti-cancer such as antiproliferation, and protect health in diet (Wahyuni et al., 2013), anti-inflammatory and antimicrobial (Sarpras et al., 2016). Several studies have been carried out to identify capsaicinoids and other metabolites such as carotenoids, phenolics, and total metabolites in *C. annuum* (Sarpras et al., 2019).

The content of bioactive compounds from chili has been known, and the use of sources of bioactive ingredients has been widely carried out. However, research studies need to be carried out to develop the potential of chili pepper in terms of treatment. This review aims to determine chili's biochemical components and pharmacological activities (*Capsicum* sp.) using the traditional review method. The scope of the evaluation in this study is that the pharmacological actions of chili pepper (*Capsicum* sp.) include: antioxidant, antimicrobial, antifungal, anti-inflammatory, anti-obesity, anti-diabetic, and dyslipidemic, while the compounds associated with these activities are: capsaicinoid alkaloids, carotenoids, peptides, phytols, fatty acids, phenolics, and flavonoids.

2. MATERIALS AND METHODS

This article review was made using the traditional review method compiled on references to previous studies. The literature was obtained from PubMed, Google Scholar, and Science Direct databases. The search for research articles that were relevant with the topic was carried out using the following keywords: "bioactive" OR "biochemical" OR "phytochemical" AND "pharmacological activity" OR "pharmacological potential" AND *Capsicum*. In addition, a search was also conducted using keywords, namely "Capcisinoid content in *capsicum* OR chili" and "compounds from *capsicum annuum* as dyslipidemia."

3. BIOACTIVE COMPOUNDS AND CHILI PEPPER ACTIVITIES

Antioxidant

Research by Olatunji et al. (2019) on the antioxidant activity of ethanolic extracts and aqueous extracts in 3 varieties of *C. annuum* (*C. annuum* var. *abbreviatum*, *C. annuum* var. *acuminatum*, *C. annuum* var. *grossum*), and one variety of *C. frutescent* (*C. frutescens* var. *baccatum*) with rutin as a standard drug. All IC_{50} values of 4 chili peppers ethanol and aqueous extracts were lowest than rutin. *C. annuum* var. *abbreviatum* is the most potent as antioxidant possessing DPPH radical scavenging activity based on IC_{50} value. In addition, the four chili peppers were showed significant scavenging activity that measured by 2,2'-Azino-Bis(3-Ethylbenzothiazoline)-6-Sulfonic Acid (ABTS) method. The ethanol and aqueous extracts of *Capsicum frutescent* var. *baccatum* were showed higher scavenging activity than standard drugs (rutin, gallic acid, and Butyl Hydroxy Toluene (BHT). *Capsicum annuum* var. *acuminatum* was showed the lowest activity in both extracts based on IC_{50} values. Meanwhile, the nitric oxide (NO) scavenging activity of Capsicum sp. showed that only ethanol extracts had antioxidant

activity. *Capsicum frutescens* var. *baccatum* has the highest activity and exhibited more potent than the reference drugs, i.e., rutin, BHT, and other extracts. The IC_{50} value of this extract was 97.1 μg/mL.

Hernandez-Ortega et al. (2012) studied antioxidant activity of different varieties from *Capsicum annuum,* i.e., guajillo, pasilla, and ancho with DPPH radical scavenging method. According to the result of this research, the antioxidant activity of guajillo pepper was higher (24.2%) than pasilla pepper (15.6%) and ancho pepper (12.3%) at a concentration of 100 μg/mL. The compound associated with the antioxidant activity was carotenoids. Based on this research, the types of carotenoids that play a role in antioxidant activity were β-carotene, capsanthin, violaxanthin, β-cryptoxanthin, zeaxanthin, lutein epoxide, capsorubin, and neoxanthin. Perez-Ambrocio et al. (2018) evaluated compounds contained in habanero chili (*C. chinense*). Based on this result, the fruits that act as antioxidants were chlorophyll, carotenoids, flavonoids, phenolic compounds, and Capsaicin. Various varieties of chili peppers are presented in **Figure 1**. Several carotenoid structures are shown in **Figure 2**.

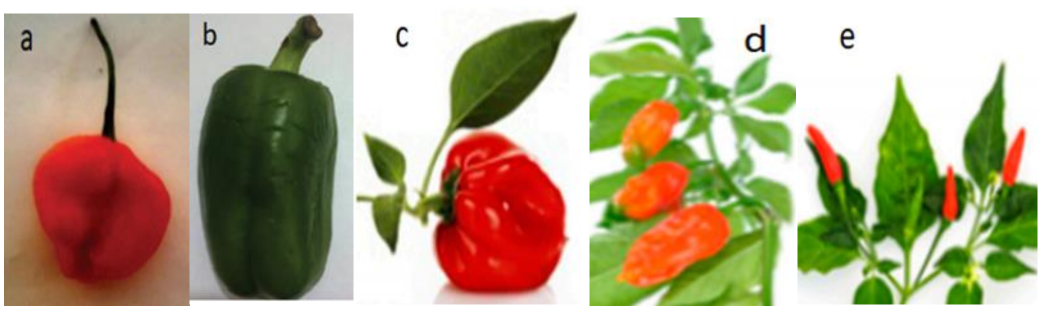

Figure 1**.** Different varieties of chili peppers: *Capsicum annuum* var. *abbreviatum* (a), *Capsicum annuum* var. *acuminatum* (b), *Capsicum annuum* (c), *Capsicum Chinense* (d), *Capsicum frutescens* (e) (Zhigila et al., 2014; Hassan et al., 2019)

Sarpras et al. (2018) studied the antioxidant activity of *C. chinense*. The result showed that the lowest dose of *C. chinense* was more effective in protecting plasmid DNA coil induced by Fenton's than a higher one. Doses of 20, 40, and 60 μg of *C. chinense* significantly increased the formation of form plasmid DNA, while higher doses of 100 μg did not protect the plasmid DNA coil. Research by Nascimento et al. (2014) uses the DPPH and ABTS methods to test the antioxidant activity of C. frutescens, Capsaicin, and dihydrocapsaicin. The antioxidant activity acetonitrile extract of seed and whole fruit of *C. frutescens* showed the best result with a percent inhibition value of 59.4% and

66.4%, which is higher than standard Trolox (55.0%). The percent inhibition of Capsaicin (51.15) and dihydrocapsaicin (54.2) was not significantly different from those with Trolox. According to Nascimento et al. (2014), there was a relationship between the total phenolic value and antioxidant activity. The highest value of total phenolic has the most potent radical scavenging activity and increased antioxidant activity. Acetonitrile extract of whole fruits had the most increased antioxidant activity, the lowest IC_{50} values in DPPH and ABTS methods, and the highest total phenolic value. There was a linear correlation between total phenolic, DPPH, and ABTS.

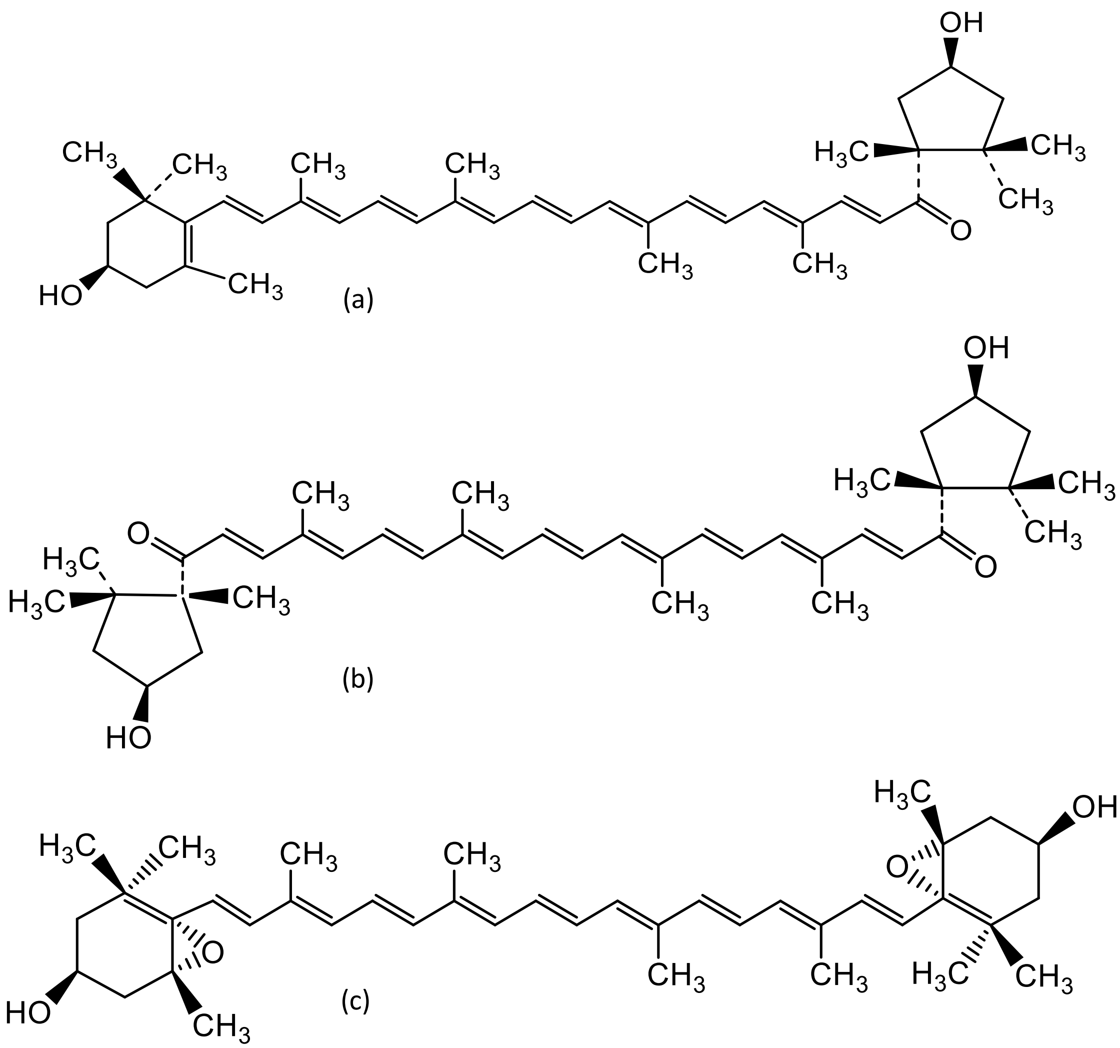

Figure 2. Structure of some carotenoids: capsanthin (a), capsorubin (b), violaxanthin (c) (Hassan et al., 2019)

Palma et al. (2020) researched enzymatic antioxidant activity with catalase and superoxide dismutase enzymes in *Capsicum annuum* varieties Metchor, Piquillo, Padrón, and Alegría, which were measured in red and green color types, respectively. Based on the study results, the catalase enzyme activity was significantly lower in ripe fruits of all varieties except the Padrón variety; its activity increased after ripening. The superoxide dismutase enzyme activity increased due to significant ripening of the Padrón and Alegría varieties. The highest activity of catalase enzyme in green *Capsicum annuum* was found in Piquillo (± 70), followed by Metchor (± 49), Padrón (± 38), and Alegría (± 37). The highest activity of the enzyme in red species was found in the Padrón variety (± 50),

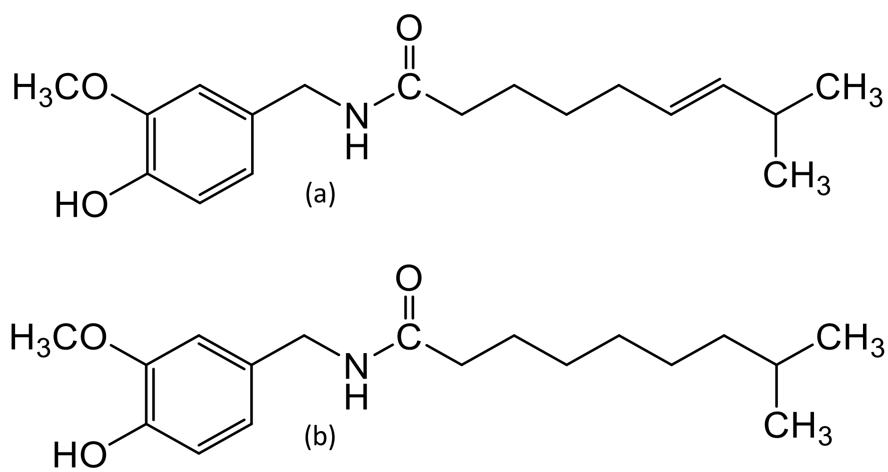

Figure 3. Structure of Capsaicin (a) and dihydrocapsaicin (b) (Imran et al., 2017)

Meanwhile, the superoxide dismutase enzyme activity in the green *Capsicum annuum* was the highest indicated by the Metchor variety (±83), followed by Piquillo and Alegría. The lowest activity was shown by Padrón (± 40). The Metchor variety demonstrated the most increased activity of this enzyme in the red array (± 105), followed by Padrón and Alegría. The Piquillo variety showed the lowest activity (± 80 units.mg^{-1} protein). Compounds that act as antioxidants in *Capsicum annuum* are capsaicinoids (Capsaicin and dihydrocapsaicin). The antioxidant activity of chili pepper (*Capsicum* sp.) is presented in **Table 1**. The structure (Capsaicin and dihydrocapsaicin is illustrated in **Figure 3**.

Table 1. Antioxidant activity of chili (*Capsicum* sp.)

Chili Pepper Species	Active Substance/ Fraction	Method	Yield (IC_{50}, mg/mL)	Reference
Capsicum annuum and *Capsicum frutescens*	Ethanol extract and water extract	**DPPH** Ethanol Extract	*Capsicum annuum* var. *abbreviatum*: 0.0779 *Capsicum annuum* var. *acuminatum*: > 0.08 *Capsicum annuum* var. *grossum* : > 0.08 *Capsicum frutescens* var. *baccatum* : 0.08 Rutin : 0.0059	Olatunji et al., 2019
		DPPH Water Extract	*Capsicum annuum* var. *abbreviatum*: 0.0523 *Cpsicum annuum* var. *acuminatum* : 0.0153 *Capsicum annuum* var. *grossum*: 0.0261 *Capsicum frutescens* var. *baccatum* : 0.0206 Rutin: 0.0059	
		ABTS Ethanol Extract	*Capsicum annum* var. *abbreviatum*: 0.033 *Capsicum annuum* var. *acuminatum* : 0.0103 *Capsicum annuum* var. *grossum* : 0.0067 *Capsicum frutesccens* var. *baccatum* : 0.0024 Rutin : 0.0057 Gallic Acid : 0.0046 BHT : 0.0074	
		ABTS Water Extract	*Capsicum annuum* var. *abbreviatum*: 0.0046 *Capsicum annuum* var. *acuminatum* : 0.0047 *Capsicum annuum* var. *grossum* : 0.0043 *Capsicum frutescens* var. *baccatum* : 0.0031 Rutin : 0.0057 Gallic Acid : 0.0046 BHT : 0.0074	
		Nitric Oxide Ethanol Extract	*Capsicum annuum* var. *abbreviatum*: 0.1803 *Capsicum annuum* var. *acuminatum* : 0.2379 *Capsicum annuum* var. *grossum* : 0.2395 *Capsicum frutesces* var. *baccatum* : 0.0971 Rutin : > 0.4 Gallic Acid :- BHT : 0.2075	
		Nitric Oxide Water Extract	*Capsicum annuum* var. *abbreviatum* : > 0.4 *Capsium annuum* var. *acuminatum* : > 0.4 *Capsicum annuum* var. *grossum* : > 0.4 *Capsicum frutescens* var. *baccatum* : > 0.4 Rutin : > 0.4 Gallic Acid :-	

			BHT : 0.2075	
		TAC Ethanol Extract	*Capsicum annuum* var. *abbreviatum*: 0.0902 *Capsicum annuum* var. *acuminatum* : 0.1636 *Capsicum annuum* var. *grossum* : 0.0951 *Capsicum frutescesns* var. *baccatum* : 0.0892 Rutin : 0.0743 Gallic Acid : 0.0485 BHT : 0.374	
		TAC Water Extract	*Capsicum annuum* var. *abbreviatum*: 0.2635 *Capsicum annuum* var. *acuminatum* : 0.2171 *Capsicum annuum* var. *grossum* : 0.3522 *Capsicum frutesccens* var. *baccatum* : 0.2651 Rutin : 0.0743 Gallic Acid : 0.0485 BHT : 0.374	
Capsicum annuum	carotenoids	DPPH	Damping capacity Guajillo : 24.2% Pasilla : 15.6% Anchos : 12.3%	Hernandez -Ortega et al., 2012
Capsicum chinense	Chlorophyll, carotenoids, flavonoids, phenolic compounds, and Capsaicin	DPPH	The regression coefficient of antioxidant strength after exposure to light: Constant : 70.7 Blue light (linear): 8.6 UV-C light (linear): 32.4 Blue light (square): -0.4 UV-C light (square): -18 Interaction of the two: -62.18 Coefficient of determination: 0.77 Habanero chili (*Capsicum Chinense*), irradiated with blue light and UV-C for 3 minutes and 0.5 minutes, increased the value of bioactive content and antioxidant power.	Perez-Ambrocio et al., 2018
Capsicum chinense	Capsaicin	DNA nicking	Small doses of Nickig DNA (20, 40, and 60 g) were more effective in protecting plasmid DNA from Fenton's inducers compared to higher doses (100 g).µ	Sarpras et al., 2018
		DPPH	Small concentrations (600 g) have more effective damping activity than large concentrations (800 g)	
		FRAP	In the FRAP test, a concentration of 140 g has better activity than a concentration of 160 g	
		DPPH	**Order from best** *Range* 23.1 to 258.6 g mL−1: ascorbic acid > capsaicin > fruit acetonitrile > dihydrocapsaicin > acetonitrile seeds > acetonitrile peel >	

Capsicum frutescens	Acetonitrile Extract		hexane fruit > hexane seeds > hexane peel	Nascimento et al., 2014
		ABTS	*Range* 24.3 to 459.6 g mL−1: trolox > capsaicin > acetonitrile fruit > acetonitrile peel > dihydrocapsaicin > hexane peel > hexane fruit > acetonitrile seeds > hexane seeds	
		Beta-carotene Assay	The percentage of beta-carotene bleaching assay: acetonitrile seeds: 59.4% fruit acetonitrile: 66.4% Trolox : 55.0% Capsaicin: 51.1% Dihydrocapsaicin: 54.2%	
Capsicum annuum	Capsaicin, dihydrocapsaicin	Enzymatic with catalase enzyme	Highest: Piquillo Lowest: Alegria Red Highest: Padron Lowest: Piquillo	Palma et al., 2020
		Enzymatic with superoxide dismutase	Green Highest: Metchor Lowest: Padron Red Highest: Metchor Lowest: Piquillo	

Antimicrobial and antifungal

Research by Koffi-Nevry et al. (2012) in the antimicrobial screening of *C. annuum* var. *antillais* has an inhibition range of 11 to 14 mm for the disc diffusion test and 11 to 21 mm for the well diffusion test. Meanwhile, the inhibition of *C. frutescens* ranged from 11 to 12 mm for the disc diffusion test, and for the well test, it was 11 to 24 mm. Both chili pepper extracts showed promising activity in aqueous and methanolic extracts, but *C. annuum* had better strength than *C. frutescens*. *Capsicum* has activity against several bacteria such as *S. aureus, salmonella,* and *V. chorelae*. However, *Capsicum* did not inhibit *Shigellae dysenteriae, Pseudomonas aeruginosa,* and *E. coli*.

Research by Gebara et al. (2020) showed the antifungal activity of *C. annuum* against the fungus *Candida* sp. and *Mycobacterium tuberculosis*. When tested by the HPLC method, Chili pepper extract was divided into six fractions. Fraction 2 (F2), fraction 3 (F3), and fraction 4 (F4) showed the highest activity in inhibiting the development of *C. buinensis* with inhibition values of 87.54%, 99.61%, and 88.41% at concentrations of 100 μg mL^{-1}. F2 and F3 also had inhibitory power when tested with *C. albican* with inhibitory power of 75.87% and 89.51%, respectively. F2 also inhibits *C. parapsilosis* with a value of 51.76% and has the highest potential as an antibiotic against *M. tuberculosis*. The inhibition value was 60% at a concentration of 100 g mL^{-1} with an MIC_{50} value of 39.2 ± 1.6 μg mL^{-1}.

The ability to inhibit *Candida* fungi was also proved by Taveira et al. (2016), who tested the inhibitory activity of *C. annuum* on various types of *Candida* fungi. *CaThi thionin-like* in chili pepper was taken and tested on *Candida* fungi. The result showed that CaThi has inhibitory activity in 6 *Candida* species. CaThi permeabilized plasma membrane in all tested fungi. Chili pepper also has broad antibacterial activity. This evident was evaluated by Vargas-Hernández et al. (2017), who tested methanolic extract of *C. chinense* on microbes. The result was obtained inhibition on three gram-positive bacteria, four gram-negative bacteria, and one fungus. The test was carried out using an antimicrobial *in vitro* method by adding foliar hydrogen peroxide, contributing to the antimicrobial activity. According to the research, capsaicinoids have antimicrobial activity and other compounds on acetonitrile and acetone extract from *C. chinense*.

Research by Nascimento et al. (2014) also showed that chili pepper has antimicrobial activity on gram-positive and negative bacteria. *C. frutescens* had antimicrobial activity against *E. coli, P. aeruginosa, K. pneumoniae, E. faecalis, B. subtilis, S. aureus,* and *Candida* fungi. Capsaicin and dihydrocapsaicin in chili pepper have antimicrobial activity, but chrysoreol did not show inhibition against *Candida* fungi. *n*-Hexane and chloroform extracts of chili pepper seeds also showed inhibitory activity on several microbes and fungi in the study of Gurnani et al. (2016). The antimicrobial and antifungal activity of chili pepper (*Capsicum* sp.) is presented in **Table 2**.

Table 2. Antimicrobial and antifungal activity of chili pepper (*Capsicum* sp.)

Chili Pepper Species/Active Substance	Method	Microorganism	Result	Reference
Capsicum annuum (water extract and methanol extract)	*Disk diffusion method* and well diffusion method	*Staphylococcus aureus*	Zone of inhibition (mm) Air disk : 11 ± 0 Methanol disk: 13 ± 0 Diffusion water: 14 ± 1.4 Methanol diffusion: 16 ± 1.4 Disc positive control : 22 ± 0 Diffusion positive control : 24 ± 0	Koffry-Nervy, et al., 2012
		Salmonella typhimurium	Air disk: 11 ± 1.4 Methanol disk : 14 ± 1.4 Diffusion water: 11 ± 1.4 Methanol diffusion: 16 ± 0 Disc positive control : 22 ± 0 Diffusion positive control : 24 ± 0	
		Vibrio cholerae	Air disk: 12 ± 0 Methanol disk: 13 ± 0 Diffusion water: 16 ± 0 Methanol diffusion : 21 ± 1.4 Disc control : 30 ± 1.4 Diffusion control: 30±1.4	
Chili Pepper Species/Active Substance	**Method**	**Microorganism**	**Result**	**Reference**

Capsicum frutescens (water extract and methanol extract)	*Disk diffusion method* and well diffusion method	*Staphylococcus aureus*	Air disk: 11 ± 1.4 Methanol disk : 12 ± 1.4 Diffusion water: 12 ± 0 Methanol diffusion: 13 ± 0 Disc positive control : 24 ± 0 Diffusion positive control: 24±0	Koffry-Nervy, et al., 2012
		Salmonella typhimurium	Air disk: 12 ± 0 Methanol disk : 12 ± 14 Diffusion water: 12 ± 0 Diffusion meth : 12 ± 1 Disc positive control : 23 ± 0 Positive control dif : .23 ± 0	
		Vibrio cholerae	Air disk: 11 ± 1.4 Methanol disk : 12 ± 0 Diffusion water: 12±0 Diffusion meth : 16 ± 01 Disc positive control : 30 ± 0 Diffusion control : 30 ± 0	
Capsicum annuum (Peptide Fraction)	*Yeast viability assay*	*Candida buinensis*	*Viability loss* (%) Control : 0 F2 : 73.67 F3 : 100 F4 : 99, 34	Gebara et al., 2020
		Candida tropicalis	Control : 0 F2 : 95.55 F3 : 97.04 F4 : 91.57	
		Candida albicans	Control : 0 F2 : 96.19 F3 : 100 F4 : 27.70	
		Candida parapsilosis	Control : 0 F2 : 53.62 F3 : 38.64 F4 : 25,30	
	Antimycobacterial assay	*Mycobacterium tuberculosis*	F2: 60% inhibition percentage at a dose of 100 g mL-1 MIC_{50} value 39.2 ± 1.6 g mL^{-1} F3: 40% inhibition percentage although unable to maintain potency after dilution. the MIC_{50} > 100 g mL^{-1}	
	Yeast viability assay	*Candida* sp.	*Viability loss* (%) *Candida albicans* : 80.3 *Candida tropicalis* : 47.9 *Candida parapsilosis*: 98.9 *Candida pelliculosa*: 70.2 *Candida buinensis* : 99.2 *Candida mogii* : 61.6	
		Candida albicans	ROS IC_{50} ($\mu g.mL^{-1}$)	

Capsicum annuum *(Thionin-like peptide)*	*ROS induction assay*		Ca-Thi : 10.0 Fluconazole : 1.0	Taveria et al., 2016
		Candida tropicalis	Ca-Thi : 10.0 Fluconazole : 1.0	
		Candida parapsilosis	Ca-Thi : 10.0 Fluconazole : 0.5	
		Candida pelliculosa	Ca-Thi : 40.0 Fluconazole : 5.0	
		Candida buinensis	Ca-Thi : 10.0 Fluconazole : 0.125	
		Candida mogii	Ca-Thi : 20.0 Fluconazole : 2.5	
Capsicum frutescens (acetonitrile extract)	*Broth-micro dilution assay*	*Enterococcus faecalis*	MIC (µg.mL-1) Capsaicin: 25 Dihydrocapsaicin: 0.6 Chrysoeriol : 1	Nascimento et al., 2014
		Bacillus subtilis	Capsaicin: 25 Dihydrocapsaicin: 1,2 Chrysoeriol : 1	
		Staphylococcus aureus	Capsaicin: 1.2 Dihydrocapsaicin: 5 Chrysoeriol : 0.25	
		Pseudomonas aeruginosa	Capsaicin: 10 Dihydrocapsaicin: 2.5 Chrysoeriol : 0.12	
		Klebsiella pneumoniae	Capsaicin: 0.6 Dihydrocapsaicin: 2.5 Chrysoeriol : 0.25	
		Escherichia coli	Capsaicin: 5 Dihydroapsaicin: 5 Chrysoeriol : 0.06	
		Candida albicans	Capsaicin: 25 Dihydrocapsaicin: 10 Chrysoeriol :-	
Capsicum frutescens	Antibacterial and antifungal test	*Escherichia coli*	Zone of inhibition (mm) *n*-Hexane : 10 ± 0.52 Chloroform : 08 ± 1.32 Positive control : 06 ± 0.34	Gurnani et al., 2015
		Salmonella typhimurium	*n*-Hexane: 5 ± 0.81 Chloroform : 06 ± 0.9 Positive control : 18 ± 1.3	
		Proteus Vulgaris	n-Hexane: 5.5 ± 1.0 Chloroform : 7 ± 0.5 Positive control: 16 ± 1.5	
		Pseudomonas aeruginosa	*n*-Hexane: 14 ± 1.3 Chloroform : 13 ± 1.7 Positive control: 10 ± 0.86	
		Klebsiella pneumoniae	*n*-Hexane: 12 ± 0.5 Chloroform: 13 ± 2.0 Positive control : 10 ± 2.59	
		Bacillus cereus	*n*-Hexane: 10 ± 1.0 Chloroform : 10 ± 1.8 Positive control : 19 ± 1.5	

(*n*-hexane and chloroform extract)		*Staphylococcus aureus*	*n*-Hexane: 14 ± 0.5 Chloroform : 15 ± 1.32 Positive control : 8 ± 0.62	
		Methicillin Resistant Staphylococcus aureus	*n*-Hexane : 5 ± 0.2 Chloroform : 0 Positive control: 13 ± 0	
		Candida albicans	*n*-Hexane: 13 ± 1.74 Chloroform : 20 ± 0.43 Positive control: 18 ± 0.90	
		Candida krusei	*n*-Hexane: 12 ± 1.03 Chloroform : 14 ± 1.51 Positive control: 11 ± 0.86	
		Alteria alternata	*n*-Hexane: 11 ± 0.62 Chloroform : 0 Positive control: 14 ± 0.45	
		Aspergillus flavus	*n*-Hexane: 0 Chloroform : 0 Positive control: 15 ± 0.33	
		Aspergillus niger	*n*-Hexane: 16 ± 1.0 Chloroform : 0 Positive control: 17 ± 0.50	

Anti-inflammatory

Hazekawa et al. (2017) researched the anti-inflammatory activity of the aqueous extract of *C. annuum* chili pepper leaves. It was concluded that the extract had anti-inflammatory activity. In previous studies, compounds that act as anti-inflammatory have been identified as Capsaicin based on HPLC chromatograms (Tang et al., 2015). However, no capsaicin compounds were found based on research conducted by Hazekawa et al. (2017) in aqueous extracts. Extract activity tested in this study also did not suppress the level of IL-6 and NF-B expression in spleen cells stimulated by Con-A. It can be concluded that Capsaicin is not responsible for anti-inflammatory activity in the aqueous extract of chili pepper leaves.

Test of carotenoids in chili pepper conducted by Hernandez-Ortega et al. (2012) showed that administration of carotenoids at doses of 5, 20, and 80 mg/kg in rats induced by acetic acid showed a significant reduction in the number of writhing with an inhibitory value of 56.4%, 47.9%, and 43.9%, respectively. Jolayemi and Ojewole (2013) gave diclofenac, Capsaicin, and ethyl acetate extract to rats and concluded that ethyl acetate extract had faster inhibitory power than diclofenac and Capsaicin. However, there was still a significant inhibition in test animals given diclofenac, Capsaicin, and ethyl

acetate extract compared to animals given albumin and water alone. Research by Boiko et al. (2019) regarding the ethanolic extract of *C. annuum* chili also has therapeutic effects as an anti-inflammatory because it showed suppression of autoimmune inflammation in mice. The anti-inflammatory activity of chili pepper (*Capsicum* sp.) is presented in **Table 3**.

Table 3. Anti-inflammatory activity of chili (Capsicum sp.)

Chili Pepper Species	Active Substance / Fraction	Method	Dose	Reference
Capsicum Annum	Water extract	Mouse spleen culture cell simulation	Dosage of bell pepper leaf water extract 1:50, 1:150 and 1:450	Hazekawa et al., 2017
Capsicum annuum	Carotenoids	Testing with rat test animals	Carotenoids: 5, 20, 80 mg/kg Ibuprofen : 10 mg/kg	Hernandez-Ortega et al., 2012
Capsicum frutescens	Ethyl acetate and capsaicin extract	Testing with rat test animals	Diclofenac : 100 mg/kg Chili pepper extract : 2.5 mg/kg Capsaicin : 2.5 mg/kg	Jolayemi and Ojewole, 2013
Capsicum annuum	Ethanol extract	Rat test animal	Ibuprofen : 50 mg/kg Chili pepper extract was made by dissolving dry chili pepper powder with 96% ethanol in a ratio of 1:4.	Boiko et al., 2019

Anti-obesity

In a double-blind, randomized study, with placebo as a control, results showed that treatment of being overweight or obese, with 6 mg per day of capsaicinoids for 12 weeks, was associated with abdominal fat loss as measured by X-ray absorption. Capsaicin may aid weight maintenance by limiting weight gain after a 5% to 10% loss. The results showed that capsaicin treatment led to sustained fat oxidation during weight maintenance compared to placebo (Zheng et al., 2017).

A prospective study was conducted to investigate the effects of Capsaicin on eating behavior and energy intake. This result shows that adding red chili for breakfast significantly reduces protein and fat intake at lunch. The addition of chili peppers to appetizers significantly reduced the cumulative energy and carbohydrate intake during lunch. This effect may be related to the increased activity of the sympathetic nervous system (Zheng et al., 2017).

The article was written by Hassan et al. (2019) regarding carotenoids in chili peppers stated that capsanthin has an anti-obesity effect on *in vitro* assays on murine preadipocyte cells adipogenesis model validated by testing on obese rats treated with a high-fat diet. Capsanthin also exhibits fatty acid-burning activity. Obese mice showed a spontaneous increase in ATP with weight loss. Beta-carotene and cryptoxanthin also play a role in adiposity activity and weight loss, although lower than capsanthin, but significantly correlate with overweight and obesity in adults and children.

Anti-diabetic

Research conducted by Tundis et al. (2013) on the anti-diabetic activity of extracts and lipophilic fractions of immature and ripe *C. annuum* fruit and various types of cultivation (Fiesta, Orange Thai, Acuminatum, Cayenne Golden). Green extract of *C. annuum* Fiesta showed the most potent α-amylase activity (IC_{50} 47.8 mg/mL). Mature *C. annuum* Fiesta extract showed no activity against α-amylase. Good α-amylase activity was also demonstrated by *C. annuum* Orange Thai with an IC_{50} of 98.7 mg/mL. The lowest α-amylase activity was found in Cayenne Golden with an IC_{50} of 222.8 mg/mL. However, Cayenne Golden showed α-glucosidase inhibition with an IC_{50} of 63.6 mg/mL. Fiesta and Orange Thai also have inhibitory activity against α-glucosidase with IC_{50} values of 109.2 mg/mL and 102.5 mg/mL, respectively.

The lipophilic fraction of *C. annuum* had α-amylase inhibitory activity. The ripening stage did not affect this activity except for *C. annuum* Fiesta, which had an IC_{50} value of 9.1 mg/mL, compared to an IC_{50} of 20.6 mg/mL when ripe. The immature phase of chili is characterized by the content of phytol and fatty acids such as myristic acid, methyl stearate, methyl linoleic, and high phenolic and flavonoid content. The flavonoid (luteolin) contained in *C. annuum* has intense α-amylase inhibitory activity. Luteolin also has α-glucosidase inhibitory activity of 36% at a 0.5 mg/mL concentration and is more potent than acarbose. Luteolin has also shown inhibitory and suppressive potential for hyperglycemia in type 2 diabetic patients.

Capsaicin has intense hypoglycemic activity involving pancreatic, insulin, hepatic and adrenal medullary secretions. A recent study showed that giving 5 grams of Capsicum frutescens to 12 healthy volunteers by performing the Oral Glucose Tolerance Test (OGTT) was associated with decreased plasma glucose levels and insulin maintenance. Both Capsaicin and dihydrocapsaicin have selective α-amylase inhibitory activity. Other researchers revealed that the compounds that have the potential as inhibitors of α-amylase and α-glucosidase are polyphenols (chlorogenic acid) and flavonoids (quercetin, rutin) (Sotto et al., 2018). A recent study showed that administering 5 grams of Capsicum frutescens to 12 healthy volunteers by performing the Oral Glucose Tolerance Test (OGTT) was associated with decreased plasma glucose levels and insulin maintenance. Both Capsaicin and dihydrocapsaicin have selective α-amylase inhibitory activity. Other researchers revealed that the compounds that have the potential as inhibitors of α-amylase and α-glucosidase are polyphenols (chlorogenic acid) and flavonoids (quercetin, rutin) (Sotto et al., 2018). A recent study showed that administering 5 grams of *Capsicum frutescens* to 12 healthy volunteers by performing the Oral Glucose Tolerance Test (OGTT) was associated with decreased plasma glucose levels and insulin maintenance. Both Capsaicin and dihydrocapsaicin have selective α-amylase inhibitory activity. Other researchers revealed that the compounds that have the potential as inhibitors of α-amylase and α-glucosidase are polyphenols (chlorogenic acid) and flavonoids (quercetin, rutin) (Sotto et al., 2018).

Research by Mohammed et al. (2017) on the activity of α-glucosidase and α-amylase of *C. annuum* various fractions (acetone, ethyl acetate, dichloromethane, n-hexane). The researcher reported that ethanolic extract of *C. annuum* acetone fraction had better inhibiting α-glucosidase and α-amylase than other fractions and acarbose. Based on these studies, the order of inhibition from the best was acetone > ethyl acetate > dichloromethane > *n*-hexane. In addition, there was a change in body weight of all animals tested; before streptozotocin (STZ) injection administration, fructose feeding did not affect the average body weight of the untreated group. After one week of STZ administration, the mean bodyweight of the animals significantly decreased compared to the non-diabetic group. However, with the acetone fraction of *C. annuum*, both doses (150 and 300 mg/kg body weight), the average weight change in the group treated with diabetes (low dose and high dose) were increased.

The administration of the acetone fraction of *C. annuum* also had no significant effect on non-diabetic animals. Data on eating and drinking of test animals in the diabetes control group significantly increased compared to normal controls. Oral administration of the acetone fraction of *C. annuum* and metformin for four weeks in diabetic rats caused a reduction in food intake and food intake. This effect was seen more clearly in the high-dose group of *C. annuum* acetone fraction compared to the low-dose group. The administration of the acetone fraction of *C. annuum* in this group did not affect the eating behavior of the rats in the non-diabetic group.

Dyslipidemia

Research on the effects of dyslipidemia due to the administration of *C. annuum* by Magied et al. (2014). A high-fructose diet induces dyslipidemia, subsequently insulin resistance, and heart failure. Treatment of *Capsicum annuum* acetone extract in diabetic rats significantly eliminated dyslipidemia by reducing total serum cholesterol, triglycerides, and Low-Density Lipoprotein (LDL) cholesterol. *C. annuum* can reduce the risk of atherogenesis and coronary artery disease, associated with decreased atherogenic index and risk index in the control group and the diabetes treatment group.

Research by Magied et al. (2014) on the effect of dry sweet red chili pepper (*Capsicum annuum*) 1%, 2%, and Capsaicin 0.015% on lipid profiles. Based on this study, serum cholesterol was significantly lower in the diabetic rats on a high lipid diet treated with 0.015% capsaicin after four weeks. Cholesterol reduction also occurred in diabetic rats on a high lipid diet with 2% dry red chili treatment. Serum triglyceride values decreased significantly after four weeks in the group of diabetic rats on a high lipid diet treated with 0.015% capsaicin and 1% and 2% dried red chili peppers. The concentration of High-Density Lipoprotein (HDL) cholesterol increased in diabetic rats on a high lipid diet with 0.015% capsaicin treatment and 2% dry red chili group. Research by Al-Jumayi et al. (2020) regarding red chili peppers (*Capsicum annuum*) it was concluded that the administration could reduce total serum cholesterol by 22-25% and 55-35% in the high lipid diet group of rats treated with 5 mg and 10 mg ethanol extract compared to the control group. In addition, there was also a significant decrease in triglyceride level and very-low-density lipoprotein (VLDL), and an increase in HDL level.

The compound responsible for dyslipidemic activity in Capsicum sp. was the carotenoid group of xanthophylls (zeaxanthin, anteraxanthin, β-cryptoxanthin, capsanthin, and capsorubin).

Compounds of this group trend to accumulate on the surface of lipoproteins. Thus, it increases the resistance of LDL cholesterol to oxidation. These compounds can prevent the critical step of the initiation and progression of atherosclerosis while enhancing HDL's function in removing excess cholesterol from the body. In addition, the carotenoid content of red chili pepper also acts as a potential natural cholesterol metabolism regulator for the prevention of atherosclerosis (Hassan et al., 2019). The anti-obesity, anti-diabetic and dyslipidemic activities of chili pepper (*Capsicum* sp.) are presented in **Table 4.**

Table 4. Anti-obesity, the anti-diabetic and dyslipidemic activity of chili (Capsicum sp.)

Chili Pepper Species	Active Substance/Fraction	Method	Dose	Reference
Capsicum annum	Capsaicin	Anti-obesity review based on rat test animals	The dose of capsaicinoid 6 mg/day for 12 weeks	Zheng et al., 2017
Capsicum p.	Carotenoids	Anti-obesity review based on animal and human testing	Dosage not listed	Hassan et al., 2019
Capsicum annuum	Chili Extract	Antidiabetic, In vitro	Extract dose: not listed	Tundis et al., 2013
Capsicum annuum	Acetone fraction	Anti-diabetic and dyslipidemia, Animal test rat	Extract dosage: 150 and 300 mg/kg	Mohammed et al., 2017
Capsicum annuum	Capsaicin	Dyslipidemia, rat test animal	Extract dose 1% and 2% Capsaicin dose 0.015%	Magied et al., 2014
Capsicum annuum	Ethanol extract	Dyslipidemia, rat test animal	Dosage of chili 5 and 10 mg	Al-Jumayi et al., 2020

Chili Pepper Nutritional Content

Chili pepper contains sugars such as glucose, fructose, sucrose, vitamin C, and organic acids such as malic acid, quinic acid, fumaric acid, citric acid, shikimic acid, and oxalic acid. Research by Zamljen et al. (2020), *C. annuum* contains more sugar (glucose = 13.9 g kg^{-1} dry matter, fructose = 28.2 g kg^{-1} dry matter, sucrose = 0.4 g kg^{-1} dry matter) than *C. chinense* at field irrigation capacity. In the field irrigation capacity method, *C. annuum* has a higher citric acid content than *C. Chinense*. Based on the theory of Forging (1986) in Zamljen et al. (2020), the concentration of citric acid will increase as drought stress increases. Several studies also mention a decrease in oxalic, quinic, shikimic, and fumaric acid concentrations in drought stress. However, Zamljen et al. (2020) resulted in the opposite study. Research by Zamljen et al. (2020) *C. annuum* concluded that vitamin C levels decreased by 20% when experiencing drought, while in *C. Chinese*, there was a 10% decrease in vitamin C levels.

According to Imran et al. (2017) mentions, *C. annum* contains many nutrients such as water, energy, carbohydrates, fiber, protein, fat, ash, calcium, iron, sodium, copper, phosphorus, selenium, magnesium, manganese, zinc, potassium, saturated fatty acids (SFA), monosaturated fatty acids (MUFA), thiamine, vitamin B6, niacin, riboflavin.

4. CONCLUSION

The content of bioactive compounds in chili pepper (*Capsicum* sp.) is alkaloids, capsaicinoid (Capsaicin, dihydrocapsaicin), carotenoids (anteraxanthin, β-carotene, capsanthin, violaxanthin, β-cryptoxanthin, zeaxanthin, lutein epoxide, capsorubin, and neoxanthin), peptides (defensin, thionin-like peptide), phytol, fatty acids (myristic acid, methyl stearic, methyl linoleic), phenolic (chlorogenic acid) and flavonoids (quercetin, luteolin, rutin). The pharmacological activities of chili pepper (*Capsicum* sp.) are antioxidant, antimicrobial, antifungal, anti-inflammatory, anti-obesity, anti-diabetic, and dyslipidemic.

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