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Striped Catfish Oil and Turmeric Extract-Reduce Inflammation and Insulin Resistance on Metabolic Syndrom: A Review

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Abstract: Metabolic Syndrome is continuing to grow worldwide. Indonesia is no exception. High-calorie diets and physical inactivity trigger several pathways involved in metabolic syndrome. These include inflammation and insulin resistance. Associated with type 2 diabetes mellitus, cardiovascular disease, and death, metabolic syndrome is important. There is therefore a need for early intervention to reduce the complications of this disease. Striped catfish (*Pangasius hypophthalmus*) is one of the freshwater fish farmed in Indonesia. Turmeric (*Curcuma longa Linn*.) is also widely used in Indonesian food preparations. This review aims to focus on striped catfish oil and turmeric extract that positively affect inflammation and insulin resistance in the intervention of metabolic syndrome. This review shows that striped catfish oil contains omega-3 fatty acids (EPA and DHA), while turmeric extract contains flavonoids, tannins, and saponins. Based on the results of the review, it is known that bioactive compounds found in catfish oil and turmeric extract can be used as nutraceutical ingredients to intervene in metabolic syndrome.

Keywords: Inflammation; Insulin resistance; Metabolic syndrome; Striped catfish oil; Turmeric extract

Introduction

Metabolic syndrome is a cluster of metabolic abnormalities. It includes central obesity, atherogenic dyslipidemia, hypertension, and insulin resistance (Rochlani et al., 2017). More than one million people worldwide are estimated to have metabolic syndrome (Saklayen, 2018). According to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), metabolic syndrome is defined as having the criteria: Waist circumference ≥ 102 cm for men, ≥ 88 cm for women; Triglyceride (TG) >150 mg/dl; HDL-C < 40 mg/dl for men, < 50 mg/dl for women; Blood pressure >130/85 mmHg; and Blood glucose ≥ 110 mg/dl or diabetic (Eckel & Cornier, 2014). The NCEP ATP III criteria were developed using measures that are accessible to clinicians. This facilitates clinical and epidemiological application. Metabolic syndrome increases the risk of type 2 diabetes, cardiovascular disease, stroke, heart attack, and death (Bovolini et al., 2020).

The inflammatory process begins as a low-grade chronic inflammatory response over a long period. It results from increased accumulation of body fat due to excessive calorie and fat intake (García-Barrado et al., 2020). Excessive growth of adipose tissue induces pro-inflammatory cytokines that activate protein kinase pathways, while at the same time stimulating macrophage infiltration and a phenotypic change from M2-type macrophages to pro-inflammatory M1-type macrophages, leading to an inflammatory state (Ramírez-Moreno et al., 2022). TNF-α (tumor necrosis factor-α) is one of the pro-inflammatory mediators strongly correlated with insulin resistance and DMT2

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pathogenesis through increased levels of CRP (C-reactive protein) and IL-6 (interleukin-6) (Akash et al., 2017). Serum levels of TNF-α are elevated in obese patients and associated with hyperinsulinemia, indicating insulin resistance in peripheral tissues (Esser et al., 2014).

Interventions for metabolic syndrome in individuals should be initiated early, without waiting for other components of metabolic syndrome to develop. This will reduce the incidence of disease complications (Chocair et al., 2022). One way is through the consumption of bioactive compounds, which are naturally present in fish oil and turmeric extract (Nurcahyanti et al., 2022; Méndez & Medina, 2021).

Fish oil contains omega-3 PUFAs: EPA and DHA, which are beneficial to human health. EPA (Eicosa Pentaenoic Acid) and DHA (Docosa Hexaenoic Acid) can be synthesized in the human body. ALA (Alpha-Linolenic Acid) is used as a precursor. However, the bioconversion of ALA to EPA and DHA is limited and requires food sources with adequate levels of omega-3 PUFA (Shahidi & Ambigaipalan, 2018). One of the Indonesian freshwater fish commodities with relatively high EPA and DHA content compared to other freshwater fish is striped catfish oil (*Pangasius hypophthalmus*) (Harmain & Dali, 2017).

Turmeric rhizome (*Curcuma longa Linn.*) is widely cultivated in Indonesia. It is used as a spice and flavoring in most food preparations (Suryawanshi et al., 2017). Previous studies have reported that turmeric extract (*Curcuma longa Linn.*) contains natural antioxidants in the form of polyphenols such as flavonoids and tannins, as well as saponins (glycoside compounds). It has the highest curcumin content (125mg/100g) of all Curcuma species (Dutta, 2015).

This review aims to focus on striped catfish oil and turmeric extract that positively affect inflammation and insulin resistance in the intervention of metabolic syndrome.

Method

A systematic search strategy was developed for the identification of studies in Google Scholar, Sciencedirect and PubMed from 2013 to 2023. The terms fish oil, striped catfish, turmeric extract, turmeric, polyphenols, inflammation, insulin resistance and metabolic syndrome were included in an electronic search strategy. To identify potentially relevant articles for this review, the authors reviewed all citations retrieved from the electronic search. In vitro data, animal data and human data were included.

Result and Discussion

Striped Catfish Oil (*Pangasius hypophthalmus*)

The Striped catfish (*Pangasius hypophthalmus*) is a freshwater fish belonging to the family Pangasiidae (Sokamte et al., 2020). The Striped catfish is a freshwater fish that is not native to Indonesia. It was first introduced in Thailand in 1972 as an ornamental fish (Harmain & Dali, 2017). Catfish contains 16.08% carbohydrates, 1.5% protein, about 5.75% fat, 0.97% ash, and 75.7% water. Catfish also contains 3.1% potassium, 0.5% phosphorus, and 3.54% Fe (Sulistyaningrum et al., 2021). Data from various literature suggest that the fatty acid profile of catfish oil is dominated by saturated fatty acids (SFA), followed by monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) (Sari et al., 2016; Ayu et al., 2019; Suseno et al., 2020). The SFA in catfish is 46% and is dominated by palmitic acid and stearic acid. The MUFA in Siamese catfish oil is omega-9 (oleic acid), which has a high percentage of 30-34%. Omega-3 (linolenic acid) and omega-6 (linoleic acid) are also found in Siamese catfish oil. Oleic, palmitoleic, and arachidonic fatty acids are characteristic of freshwater fish oil, as indicated by its semisolid texture at room temperatures (Yi et al., 2014).

Striped catfish is a good source of omega-3 PUFA (EPA and DHA). Striped catfish stomach contents (digestive tract, liver, bile, and abdominal fat) have greater potential as a source of fat rich in omega-3 PUFAs (EPA and DHA). However, processing by combining stomach contents with fish flesh parts may increase the oxidation and hydrolysis of fish fat (Manthey-Karl et al., 2016). Skin fillets are another source of omega-3 PUFAs (Reski et al., 2021).

Omega-3 PUFA content of catfish can be obtained by extraction followed by purification to obtain fish oil suitable for human consumption according to IFOS standards, namely peroxide number ≤ 3.75 meq/kg and free fatty acids < 1.50% (Lima et al., 2023) (Figure 1). One extraction method that is often used is the wet extraction method because it gives a higher oil yield. The purification process can be carried out by several methods, namely alkaline (NaOH) purification, acid purification, physical purification, and adsorption purification. Bentonite adsorbent can be used as a bleaching agent in the oil refining process due to its high montmorillonite content (Sembiring et al., 2018).

Figure 1. Process for obtaining omega-3 PUFAs (EPA and DHA) components from striped catfish oil (*Pangasius hypophthalmus*)

Omega-3 PUFA and Metabolic Syndrome

Omega-3 PUFAs are polyunsaturated fatty acids (PUFAs) characterized by the presence of the first broken methylene double bond at the third carbon atom of the methyl end of the fatty acid chain (Tortosa-caparrós et al., 2016). Omega-3 PUFAs consist of alpha-linolenic acid (ALA; 18:3 ω-3), stearidonic acid (SDA; 18:4 ω-3), eicosapentaenoic acid (EPA; 20:5 ω-3), docosapentaenoic acid (DPA; 22:5 ω-3) and docosahexaenoic acid (DHA; 22:6 ω-3). The human body is unable to synthesize all of these omega-3 PUFAs due to a limitation in the enzyme responsible for the insertion of the cis double bond. The concentration of EPA and DHA in the cell membrane is important for the structural function of the cell (Dupont et al., 2019). ALA is an essential unsaturated fatty acid with carbon. It is converted to EPA or DPA by chain elongation and desaturation. EPA and DHA can be synthesized in the human body by using ALA as a precursor for the synthesis. However, the bioconversion of ALA to EPA and DHA is limited. Therefore, dietary sources with adequate levels of omega-3 PUFA are required (Shahidi & Ambigaipalan, 2018).

The main sources of ALA are plant sources in seeds, nuts, and some vegetable oils such as flaxseed, chia seeds, and walnuts. EPA and DHA are abundant in fatty fish and seafood. The 2015 Dietary Guidelines for Americans recommend eating about 8 ounces of seafood per week. This would provide about 250 mg/day of EPA and DHA. Levels of omega-3 PUFA up to 3g/day are generally considered safe by the US Food and Drug Administration (U.S. Department of Health and Human Services & U.S. Department of Agriculture, 2015). Dietary intake of omega-3 PUFA sources has been shown to play a role in cardiovascular risk reduction by consuming at least 1-2 servings of fish per week; in particular, high levels of EPA and DHA are associated with a reduced risk of coronary death and all-cause mortality, so the AHA (American Heart Association) recommends consuming at least two servings of fish per week. DHA and EPA are also needed to grow the brain and retina for normal nerve function and vision (Backes et al., 2016).

The importance of omega-3 PUFAs for health is related to their role as metabolic precursors of eicosanoids. Eicosanoids are a family of signaling molecules that play an important role in the regulation of inflammatory processes. EPA and DHA are the most important omega-3 PUFAs. They can modify gene expression and anti-inflammatory processes. Previous research has reported that omega-3 PUFAs are ligands for G-120 protein-coupled receptors, which reduce TNF-α-mediated pro-inflammatory signaling in macrophages (Table 1). Thus, omega-3 PUFAs attenuate TNF-α levels by suppressing macrophage-induced tissue inflammation, and such anti-inflammatory activity can inhibit triglyceride synthesis (Pahlavani et al., 2020).

EPA and DHA alter several metabolic processes, including carbohydrate and lipid metabolism, which are largely mediated by the transcription factor peroxisomal proliferator-activated receptor (PPAR), with two receptor subtypes, PPARα and PPARγ. PPARγ mediates the effects of EPA and DHA on adiponectin up-regulation. PPARα mediates the beneficial effects of EPA on hepatic insulin sensitivity. Omega-3 PUFAs shift fat from the synthetic to the oxidative pathway by increasing fatty acid oxidation and inhibiting the transcription of hepatic and adipose lipogenic genes (Sasanfar et al., 2024).

Omega-3 PUFAs exert their protective effects through the AMPK stimulation pathway, in addition to the stimulation of PPARs. In Sprague-Dawley rats fed a high glucose diet and given an omega-3 PUFA-rich fish oil intervention, there was a two- to threefold increase in hepatic AMPK phosphorylation. EPA and DHA influence fatty acid oxidation and reduce adiposity. This makes them ideal bioactive dietary compounds for the treatment of metabolic syndrome (Parunyakul et al., 2022).

Table 1. Effects of Omega-3 PUFAs in Preclinical Animal Studies and Clinical Trials

Compound	Subjects	Dose	Mechanism of Action	References
Omega-3 (*Pangasius hypophtalamus fish oil*)	Malnourished Wistar rats.	0.060ml/200g BW/day	Catfish (*Pangasius hypophtalamus fish)* oil supplementation for 3 weeks can reduce levels of the pro-inflammatory cytokine hs-CRP in malnourished Wistar rats.	Reski et al. (2021)
Omega-3 (*Pangasius hypophtalamus* Fish Oil Extract)	Male white rats (*Rattus novergicus*) with alloxan injection	72.8 mg/kg BW	Patin Fish Oil Extract given to rats for 7 days was shown to affect the blood glucose profile	Hidayaturrahmah et al. (2017)
Omega-3 (Fish oil supplement)	Patient with schizophrenia	720 mg EPA and 480 mg DHA/day	Fish oil supplementation for 12 weeks can reduce TNF-α levels. The reduction in TNF-α levels was accompanied by a reduction in triglyceride levels. Both were positively correlated.	Xu et al. (2018a)
Omega-3 (Fish oil supplement)	Humans with insulin resistance	4 mg/day	Fish oil supplementation for 12 weeks reduced adipose tissue macrophages, increased adipose tissue capillaries, and reduced the pro-inflammatory cytokine MCP-1.	Spencer et al. (2013)
Omega-3 (Fish oil supplement)	Male C57BL/6 mice with metabolic syndrome	2 g/kg BW	Fish oil supplementation 3 times a week for 8 weeks reduced body weight, glucose, and lipolysis.	Sá et al. (2020)

Turmeric Extract

Turmeric (*Curcuma longa Linn*. syn. *Curcuma domestica Val*.) has rhizomes and is a member of the ginger family. In Asia and other tropical countries, turmeric is widely cultivated. Turmeric has long been used in Asia as a spice and flavoring in most foods (Amalraj et al., 2017). Turmeric plants are ready to harvest when they are 8-18 months old. The best time to harvest is when the plant is 11-12 months old, marked by the fall of the second leaf. Turmeric harvested at 11-12 months of age produces a greater and more abundant turmeric production than turmeric harvested at 7-8 months of age. The highest yield of 23.63%, antioxidant capacity of 6.60 (mg GAEAC/100 g sample), and total phenolics of 24.03 (mg GAE/100 g sample) can be obtained from turmeric harvested at 11 months of age (Dewi et al., 2016).

The chemical composition of turmeric is approximately 70% carbs, 13% air, 6% protein, 6% essential oils (phellandrene, sabinene, cineol, borneol, zingiberene, and sesquiterpenes), 5% fat, 3% minerals (potassium, calcium, phosphorus, iron, and sodium), small amounts of vitamins (B1, B2, C, and niacin), and 3-9% curcuminoids (Kotha & Luthria, 2019). Curcuminoids are the compounds that give the yellow-orange color to the rhizomes of the turmeric plant (Rezki et al., 2015). Curcuminoids are made up of curcumin, demethoxy curcumin and bis-demethoxy curcumin. Turmeric also contains several secondary metabolites, namely alkaloids, terpenoids, phenols, flavonoids, tannins, and saponins. Turmeric has the highest curcumin content (125 mg/100g) compared to other Curcuma genera (C. amada, C. caesia, C. angustifolia, C. leucorrhiza, C. longa and C. zedoaria) (Dutta, 2015).

Extraction methods can be used to determine the content of secondary metabolites in turmeric extract (Figure 2). Extraction methods that can be used for the extraction of active compounds from turmeric are maceration, percolation, and soxhletation. One of the most commonly used extraction methods for turmeric is the maceration method (Llano et al., 2022). The maceration method is the simplest extraction method; it does not use high temperatures during the extraction process, so it does not damage heat-resistant substances such as curcumin; it is cheap and easy to carry out; and it uses simple equipment to obtain the desired compound. A solvent that can be used in the extraction is ethanol. Ethanol is polar and has the property of attracting secondary metabolites in simplicia in optimal amounts (Venkateshwari et al., 2021).

The turmeric extract obtained from the maceration process can be further processed by freeze drying, the aim of which is to obtain an extract that is stable in storage and maintains the quality of the extract so that it can be made into a preparation that is safe for consumption. Freeze-drying is a method of preserving products by freezing them and then drying/sublimation them in a vacuum (Park et al., 2022).

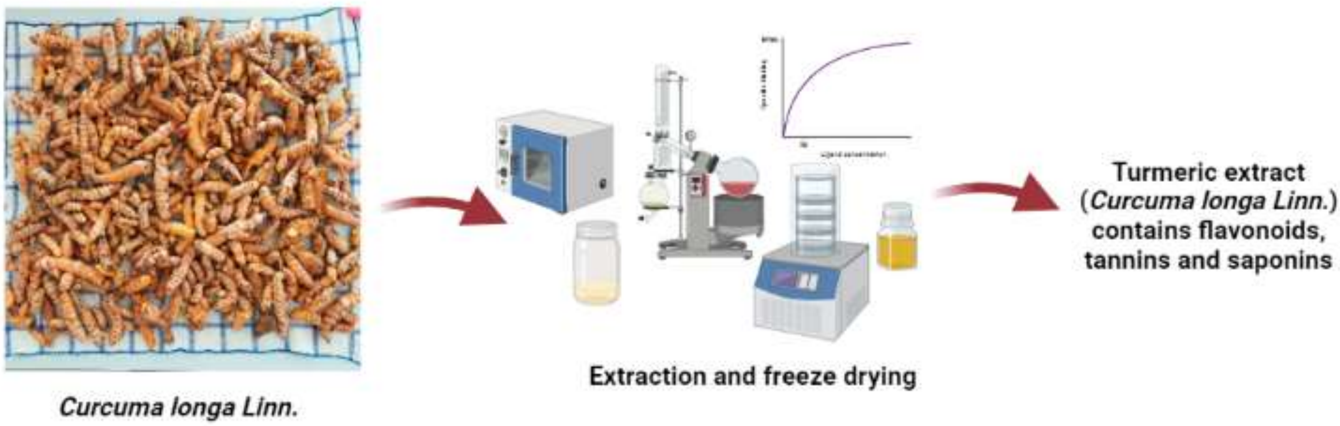

Figure 2. Process for obtaining flavonoids, tannins, and saponins components from turmeric extract (*Curcuma longa* Linn.)

Secondary Metabolites (Flavonoids, Tannins, Saponins) and Metabolic Syndrome

Low-grade inflammation and oxidative stress in the mitochondria as a result of obesity are partly responsible for insulin resistance. Increased pro-inflammatory cytokines may alter the metabolic homeostatic control system leading to DMT2 (Keane et al., 2015). Antioxidants can protect tissues from free radical damage. They can inhibit radical synthesis, scavenge free radicals, or accelerate their damage. Therefore, to maintain good physiological function, a balance between free radical and antioxidant concentrations is required (Mohajeri et al., 2021).

Plants, the biological activity of which is influenced by the presence of secondary metabolites (Agustina et al., 2017). Plant-derived secondary metabolites are produced to support and enhance plant growth. Photosynthesis, glycolysis, and the Krebs cycle produce these metabolites (Bernardini et al., 2018; Suaifan et al., 2015). All Curcuma genera, including Curcuma longa Linn, contain alkaloids, flavonoids, terpenoids, phenols, tannins, and saponins. Several studies have shown that polyphenolic compounds such as flavonoids, phenolic acids, and tannins are potential antioxidants. The antioxidant activity of these compounds is due to their ability to scavenge free radicals. Turmeric ethanol extract has a greater antioxidant effect than turmeric water extract. It protects against free radical damage (Tanvir et al., 2017).

Polyphenols are secondary plant metabolites with characteristic aromatic rings containing one or more hydroxy (OH) groups. These polyphenolic compounds are readily soluble in polar solvents, oxidize to dark color in the air, oxidize readily with strong bases, complex with proteins, are sensitive to enzymatic oxidation, and absorb UV-Vis light. Polyphenolic compounds are made up of several groups, namely the simple phenols and phenolic acids, the phenylpropanoids, the flavonoids, and the tannins (Julianto, 2019). The number and arrangement of hydroxyl groups in the molecules studied determine the antioxidant potential of polyphenolic compounds. Polyphenolic antioxidants can donate hydrogen atoms to lipid radicals, producing lipid derivatives and antioxidants that are more stable and less available to promote autoxidation (a free radical chain reaction between unsaturated fatty acids and oxygen to form hydroperoxides). The ability of polyphenolic compounds, including flavonoids, to directly scavenge free radicals is a potential mechanism for their protective effects (Gu et al., 2020).

Flavonoids are potent scavengers of reactive species. These include superoxide, peroxyl radicals, and peroxynitrite. By scavenging these reactive species, flavonoids prevent the formation of highly reactive oxygen species and limit the progression of oxidative reactions. Flavonoids may inhibit the production of inflammatory cytokines such as TNF-α, IL-1β, IL-6, and interferon-γ, as well as chemotactic agents. Flavonoids are also anti-diabetic. They act on the insulin receptor, protein tyrosine phosphatase, peroxisome proliferator-activated receptor, and adenosine monophosphate-activated protein kinase (Islam et al., 2020).

Tannins are polyphenolic compounds that give a bitter and astringent taste. They can react with and coagulate proteins or other organic compounds containing amino acids and alkaloids. Tannins have several health benefits. These include scavenging free radicals and acting as antioxidant enzyme activators. Benefits include controlling and managing chronic diseases including diabetes. Tannin enhances insulin signaling pathways such as activation of PI3K (phosphoinositide 3-kinase), p38 MAPK (mitogen-activated protein kinase), and GLUT-4 translocation. This results in increased glucose absorption. It also reduces the intestinal absorption of glucose and other nutrients, induces beta-cell regeneration, inhibits alphaamylase and alpha-glucosidase activity, and increases insulin activity in adipocytes (Alhujaily et al., 2022). Tannins can inhibit the growth of many fungi, yeasts, and bacteria. They also have analgesic and anti-inflammatory properties (Shehadeh et al., 2021).

Saponin is a glycoside compound. It is a secondary metabolite that binds to sugar compounds through glycosidic bonds. Saponin compounds have antioxidant activity. Saponins can reduce superoxide through the formation of hyperoxide intermediates, thus preventing biomolecular damage by free radicals (Hasan et al., 2022). This compound has strong biological activity and antihyperglycaemic activity (Bharti et al., 2018). Saponin is an inhibitor of the α-glucosidase enzyme. The α-glucosidase enzyme is an enzyme whose role is to convert carbohydrates into glucose. Therefore, inhibiting the work of the α-glucosidase enzyme can reduce glucose (sugar) levels in the blood and cause a hypoglycaemic (low blood sugar) effect. Saponin causes permanent blistering in contact with water. This compound is also a cause of hemolysis in red blood cells. Saponins have anti-carcinogenic properties due to their immunomodulatory effects (Xu et al., 2018b). Based on previous studies, secondary metabolites (flavonoids, tannins, and saponins) from turmeric extract have anti-inflammatory and antihyperglycaemic effects (Table 2).

Table 2. Effects of Turmeric Extract in Cell Culture Studies and Clinical Trials

Compound	Subjects	Dose	Mechanism of Action	References
Water extract Curcuma (WEC)	Human umbilical vascular endothelial cells (HUVECs)	800 μg/mL	WEC significantly suppressed both TNF-α-induced protein expression of adhesion molecules and monocyte adhesion. WEC inhibits the NF-κB signaling pathway	Kawasaki et al. (2015)
Water extract Curcuma (WEC)	Subjects with overweight or prehypertension	900 mg/day	Administration of WEC for 12 weeks significantly reduced serum levels of pro-inflammatory mediators (CRP, TNF-α, IL-6)	Uchio et al. (2019)
Water extract Curcuma (WEC)	Subjects with overweight or prehypertension	900 mg/day	Administration of WEC for 12 weeks significantly reduced serum hsCRP and fasting serum glucose levels	Uchio et al. (2022)

Combination Effects of Fish Oil and Polyphenols

Fish oil is susceptible to oxidizing. The high number of double bonds and their position in the fatty acid chain make omega-3 PUFAs susceptible to oxidation. Structures containing two or more 1,4-diene systems easily lose hydrogen, leading to the onset of oxidation. Oxidation in fish oil is prevented by using natural antioxidants, which are more beneficial to use. Antioxidants can inhibit oxidation reactions by binding free radicals and highly reactive molecules. This prevents cell damage. Natural antioxidants can be derived from polyphenolic compounds with antioxidant activity, often found in spices, which can inhibit the growth of undesirable microorganisms in foods and/or prevent the formation of toxic substances such as heterocyclic amines (Hrebień-Filisińska, 2021).

Turmeric extract (*Curcuma longa Linn.*) is a source of natural antioxidants. Previous studies have reported that catfish oil (*Pangasius hypophthalmus*) with the addition of turmeric extract (*Curcuma longa Linn.*) had lower levels of peroxides and free fatty acids after 7 days of storage than catfish oil without the addition of turmeric extract (Nasution et al., 2021). The combination of polyphenols and omega-3 PUFAs mutually influence their pharmacological profile and bioavailability because polyphenols prevent oxidation of omega-3 PUFAs, thereby facilitating intestinal absorption while maintaining their bioactivity and omega-3 PUFAs influence the metabolism and bioaccessibility of polyphenols and, if conjugated, omega-3 PUFAs and polyphenols (as lipophenols) can provide several advantages, including increasing the lipophilicity, cell penetration and bioavailability of specific polar phenolic drugs, achieving appropriate solubility of hydrophobic drugs, limiting the autoxidation of PUFA conjugates and covering their polar hydroxyl function, thereby reducing biotransformation or degradation rates. Oxidation and thus increase the antioxidant properties (Crauste et al., 2015).

Previous in vitro studies reported synergistic anti-inflammatory effects of low-dose curcumin combined with DHA or EPA not only inhibited NO production in LPS-stimulated RAW 264.7 cells but also inhibited non-LPS-treated cells. The induction of antioxidants attenuates LPS-mediated ROS production, resulting in reduced iNOS and NO production. When combined with DHA or EPA, the anti-inflammatory and antioxidant activities of curcumin can be synergistically enhanced (Martínez et al., 2018).

Another study also reported a 3-fold reduction in nuclear β-catenin in aberrant crypt foci compared to controls in mice with colon tumors given 1% curcumin and 4% fish oil for 3 weeks. Omega-3 PUFA plus curcumin synergistically increased the number of apoptotic targets in DNA-damaging Lg5+20 (leucine-rich repeat-containing G-protein-coupled receptor 5-

positive) stem cells by 4.5 times compared to controls (Kim et al., 2016). Separately, other research has reported that fish oil rich in omega-3 PUFA combined with the polyphenol curcumin increased oxidative stress protective proteins and anabolic signaling in the soleus muscle of rats, thereby reducing muscle atrophy (Lawler et al., 2018).

Constraint

There are not many preliminary studies looking at the mechanism of secondary metabolites (flavonoids, tannins, and saponins) in turmeric extracts in metabolic syndrome subjects. The results may lead to plans to conduct preclinical trials to see the effect of these secondary metabolite levels on the improvement of metabolic syndrome.

Conclusion

Bioactive compounds with the ability to improve inflammatory responses and insulin resistance are found in striped catfish oil (*Pangasius hypophthalmus*) and turmeric extract (*Curcuma longa Linn*.). These two ingredients have the potential to be used as nutraceutical ingredients in the metabolic syndrome. Therefore, this review is in favor of preclinical research in experimental animals. The complementary effects of the two bioactive compounds can also be evaluated using pre-clinical studies.

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Conceptualization, methodology, and writing—original draft preparation, H.D.M.; validation, formal analysis, investigation, writing—review and editing, and supervision, M.M., M. S., and D.N.A.

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Conflicts of Interest
The authors declare no conflict of interest.

References

Agustina, W., Nurhamidah, N., & Handayani, D. (2017). Skrining Fitokimia dan Aktivitas Antioksidan Beberapa Fraksi dari Kulit Batang Jarak (Ricinus communis L.). *Jurnal Pendidikan dan Ilmu Kimia*, *1*(2), 117–122. https://doi.org/10.33369/atp.v1i2.3529

Akash, M. S. H., Rehman, K., & Liaqat, A. (2017). Tumor Necrosis Factor-Alpha: Role in Development of Insulin Resistance and Pathogenesis of Type 2 Diabetes Mellitus. *Journal of Cellular Biochemistry*, 1–16. https://doi.org/10.1002/jcb.26174

Alhujaily, M., Dhifi, W., & Mnif, W. (2022). An Overview of the Potential of Medicinal Plants Used in the Development of Nutraceuticals for the Management of Diabetes Mellitus: Proposed Biological Mechanisms. *Processes*, *10*(2044), 1–20. https://doi.org/10.3390/pr10102044

Amalraj, A., Pius, A., Gopi, S., & Gopi, S. (2017). Biological Activities of Curcuminoids, Other Biomolecules from Turmeric and Their Derivatives e A Review. *Journal of Traditional and Complementary Medicine*, *7*, 205–233. https://doi.org/10.1016/j.jtcme.2016.05.005

Ayu, D. F., Diharmi, A., & Ali, A. (2019). Characterization of the Oil from the Abdomen Part of Smoked Catfish (Pangasius hypophthalmus) Processing by-Product (Pangasius hypophthalmus). *Jurnal Pengolahan Hasil Perikanan Indonesia*, *22*(1), 187–197. https://doi.org/10.17844/jphpi.v22i1.26473

Backes, J., Anzalone, D., Hilleman, D., & Catini, J. (2016). The Clinical Relevance of Omega-3 Fatty Acids in the Management of Hypertriglyceridemia. *Lipids in Health and Disease*, *15*(118), 1–12. https://doi.org/10.1186/s12944-016-0286-4

Bernardini, S., Tiezzi, A., Masci, V. L., & Ovidi, E. (2018). Natural Products for Human Health: A Historical Overview of the Drug Discovery Approaches. *Natural Product Research*, *32*(16), 1926–1950. https://doi.org/10.1080/14786419.2017.1356838

Bharti, S. K., Krishnan, S., Kumar, A., & Kumar, A. (2018). Antidiabetic Phytoconstituents and Their Mode of Action on Metabolic Pathways. *Therapeutic Advances in Endocrinology and Metabolism Review*, *9*(3), 81–100. https://doi.org/10.1177/2042018818755019

Bovolini, A., Garcia, J., Andrade, M. A., & Duarte, J. A. (2020). Metabolic Syndrome Pathophysiology and Predisposing Factors. *Int J Sports Med*. https://doi.org/10.1055/a-1263-0898

Chocair, P. R., Neves, P. D. M. D. M., Sato, V. A. H., Mohrbacher, S., Oliveira, É. S., Pereira, L. V. B., Bales, A. M., Silva, F. P. D., Duley, J. A., & Cuvello-Neto, A. L. (2022). Proposal for Standardizing Normal Insulin Ranges in Brazilian Patients and a New Classification of Metabolic Syndrome. *Frontiers in Medicine*, *9*(984001), 1–9. https://doi.org/10.3389/fmed.2022.984001

Crauste, C., M, R., Thierry, D., & Joseph, V. (2015). Omega-3 Polyunsaturated Lipophenols, How and Why? *Biochimie*, *120*, 62-74. https://doi.org/10.1016/j.biochi.2015.07.018

Dewi, P. J. N., Hartiati, A., & Mulyani, S. (2016). Pengaruh Umur Panen dan Tingkat Maserasi Terhadap Kandungan Kurkumin dan Aktivitas Antioksidan Ekstrak Kunyit (Curcuma domestica Val.). *Jurnal Rekayasa dan Manajemen Agroindustri*, *4*(3), 105–115. Retrieved from https://garuda.kemdikbud.go.id/documents/detail/1351364

Dupont, J., Dedeyne, L., Dalle, S., Koppo, K., & Gielen, E. (2019). The Role of Omega-3 in the Prevention and Treatment of Sarcopenia. *Aging Clinical and Experimental Research*, *31*, 825–836. https://doi.org/10.1007/s40520-019-01146-1

Dutta, B. (2015). Study of Secondary Metabolite Constituents and Curcumin Contents of Six Different Species of Genus Curcuma. *Journal of Medicinal Plants Studies*, *3*(5), 116–119. Retrieved from https://www.plantsjournal.com/archives/2015/vol3issue5/PartB/3-5-10.pdf

Eckel, R. H., & Cornier, M. (2014). Update on the NCEP ATP-III Emerging Cardiometabolic Risk Factors. *BMC Medicine*, *12*(115), 1–9. Retrieved from http://www.biomedcentral.com/1741-7015/12/115

Esser, N., Legrand-poels, S., Piette, J., Scheen, A. J., & Paquot, N. (2014). Inflammation as a Link between Obesity, Metabolic Syndrome, and Type 2 Diabetes. *Diabetes Research and Clinical Practice*, 1–25. https://doi.org/10.1016/j.diabres.2014.04.006

García-Barrado, M. J., Iglesias-Osma, M. C., Pérez-García, E., Carrero, S., Blanco, E. J., Carretero-Hernández, M., & Carretero, J. (2020). Role of Flavonoids in the Interactions Among Obesity, Inflammation, and Autophagy. *Pharmaceuticals*, *13*(342), 1–26. https://doi.org/10.3390/ph13110342

Gu, C., Suleria, H. A. R., Dunshea, F. R., & Howell, K. (2020). Dietary Lipids Influence Bioaccessibility of Polyphenols from Black Carrots and Affect Microbial Diversity under Simulated Gastrointestinal Digestion. *Antioxidants*, *9*(762), 1–17. https://doi.org/10.3390/antiox9080762

Harmain, R. M., & Dali, F. A. (2017). *Buku Ajar Ilabulo Ikan Patin (Pangasius, sp.)*. Gorontalo: UNG Press Gorontalo.

Hasan, H., Thomas, N. A., Hiola, F., Ramadhani, F. N., & Ibrahim, P. A. S. (2022). Skrining Fitokimia dan Uji Aktivitas Antioksidan Kulit Batang Matoa (Pometia pinnata) dengan Metode 1, 1-Diphenyl-2 picrylhidrazyl (DPPH). *Indonesian Journal of Pharmaceutical Education (e-Journal)*, *2*(1), 52–66. https://doi.org/10.37311/ijpe.v2i1.10995

Hidayaturrahmah, H., Santoso, H. B., & Nurlely, N. (2017). Profil Glukosa Darah Tikus Putih Setelah Pemberian Ekstrak Minyak Ikan Patin (Pangasius hypopthalmus) sebagai Alternatif Antidiabetes. *Jurnal Pharmascience*, *04*(02), 219–226. http://dx.doi.org/10.20527/jps.v4i2.5775

Hrebień-Filisińska, A. (2021). Application of Natural Antioxidants in the Oxidative Stabilization of Fish Oils: A Mini-Review. *Journal of Food Processing and Preservation*, *45*(e15342), 1–12. https://doi.org/10.1111/jfpp.15342

Islam, A., Islam, S., Rahman, K., Uddin, N., & Akanda, R. (2020). The Pharmacological and Biological Roles of Eriodictyol. *Archives of Pharmacal Research*, 1–11. https://doi.org/10.1007/s12272-020-01243-0

Julianto, T. S. (2019). *Fitokimia Tinjauan Metabolit Sekunder dan Skrining fitokimia*. Jakarta: Penerbit buku kedokteran EGC.

Kawasaki, K., Muroyama, K., Yamamoto, N., & Murosaki, S. (2015). A Hot Water Extract of Curcuma longa Inhibits Adhesion Molecule Protein Expression and Monocyte Adhesion to TNF-α-Stimulated Human Endothelial Cells. *Bioscience, Biotechnology, and Biochemistry*, *79*(10), 1654–1659. https://doi.org/10.1080/09168451.2015.1039480

Keane, K. N., Cruzat, V. F., Carlessi, R., Jr., P. I. H. de B., & Newsholme, P. (2015). Molecular Events Linking Oxidative Stress and Inflammation to Insulin Resistance and ? -Cell Dysfunction. *Oxidative Medicine and Cellular Longevity*, 1–15. https://doi.org/10.1155/2015/181643

Kim, E., Davidson, L. A., Zoh, R. S., Hensel, M. E., Salinas, M. L., Patil, B. S., Jayaprakasha, G. K., Callaway, E. S., Allred, C. D., Turner, N. D., Weeks, B. R., & Chapkin, R. S. (2016). Rapidly Cycling Lgr5 + Stem Cells Are Exquisitely Sensitive to Extrinsic Dietary Factors That Modulate Colon Cancer Risk. *Cell Death and Disease*, *7*(e2460), 1–14. https://doi.org/10.1038/cddis.2016.269

Kotha, R. R., & Luthria, D. L. (2019). Curcumin: Biological, Pharmaceutical, Nutraceutical, and Analytical Aspects. *Molecules*, *24*(2930), 1–27. https://doi.org/10.3390/molecules24162930

Lawler, J. M., Garcia-villatoro, E. L., Guzzoni, V., Hord, J. M., Botchlett, R., Holly, D., Lawler, M. S., Gomes, M. J., Ryan, P., Rodriguez, D., Kuczmarski, J. M., Fluckey, J. D., & Talcott, S. (2018). Effect of Combined Fish Oil & Curcumin on Murine Skeletal Muscle Morphology and Stress Response Proteins During Mechanical Unloading. *Nutrition Research*, *65*, 17–28. https://doi.org/10.1016/j.nutres.2018.12.013

Lima, R. A. M., Ferraz, S. M. M., Cardoso, V. G. K., Teixeira, C. A., & Hantao, L. W. (2023). Authentication of Fish Oil (Omega-3) Supplements

Using Class-Oriented Chemometrics and Comprehensive Two-Dimensional Gas Chromatography Coupled to Mass Spectrometry. *Analytical and Bioanalytical Chemistry*, *415*, 2601–2611. https://doi.org/10.1007/s00216-022-04428-2

Llano, S. M., Gómez, A. M., & Duarte-Correa, Y. (2022). Effect of Drying Methods and Processing Conditions on the Quality of Curcuma longa Powder. *Processes*, *10*(702), 1–15. https://doi.org/10.3390/pr10040702

Manthey-Karl, M., Lehmann, I., Ostermeyer, U., & Schröder, U. (2016). Natural Chemical Composition of Commercial Fish Species: Characterisation of Pangasius, Wild and Farmed Turbot and Barramundi. *Foods*, *5*(58), 1–14. https://doi.org/10.3390/foods5030058

Martínez, N., Herrera, M., Frías, L., Provencio, M., Pérez ‑Carrión, R., Díaz, V., Morse, M., & Crespo, M. C. (2018). A Combination of Hydroxytyrosol, Omega ‑3 Fatty Acids and Curcumin Improves Pain and Inflammation Among Early Stage Breast Cancer Patients Receiving Adjuvant Hormonal Therapy: Results of a Pilot Study. *Clinical and Translational Oncology*, *21*, 489–498. https://doi.org/10.1007/s12094-018-1950-0

Méndez, L., & Medina, I. (2021). Polyphenols and Fish Oils for Improving Metabolic Health: A Revision of the Recent Evidence for Their Combined Nutraceutical Effects. *Molecules*, *26*(2438), 1–24. https://doi.org/10.3390/molecules26092438

Mohajeri, M., Behnam, B., Tasbandi, A., Jamialahmadi, T., & Sahebkar, A. (2021). Carbon-Based Nanomaterials and Curcumin: A Review of Biosensing Applications. In P. C. Guest (Ed.), *Studies on Biomarkers and New Targets in Aging Research in Iran Focus on Turmeric and Curcumin* (pp. 55–74). https://doi.org/10.1007/978-3-030-56153-6_4

Nasution, A. Y., Novalia, W., & Sari, D. A. (2021). Evaluasi Karakteristik Minyak Ikan Patin (Pangasius hypophthalmus) dengan Penambahan Ekstrak Kunyit sebagai Antioksidan Alami. *Jurnal Ilmiah Farmasi Farmasyifa*, *4*(2), 22–28. https://doi.org/10.29313/jiff.v4i2.6915

Nurcahyanti, A. D. R., Cokro, F., Wulanjati, M. P., Mahmoud, M. F., Wink, M., & Sobeh, M. (2022). Curcuminoids for Metabolic Syndrome : Meta-Analysis Evidences Toward Personalized Prevention and Treatment Management. *Frontiers in Nutrition*, *9*(June), 1–19. https://doi.org/10.3389/fnut.2022.891339

Pahlavani, M., Ramalho, T., Koboziev, I., Lemieux, M. J., Jayarathne, S., Ramalingam, L., Filgueiras, L. R., & Moustaid-moussa, N. (2020). Adipose Tissue Inflammation in Insulin Resistance: Review of Mechanisms Mediating Anti-Inflammatory Effects of Omega-3 Polyunsaturated Fatty Acids. *J Investig Med*, *65*(7), 1021–1027. https://doi.org/10.1136/jim-2017-000535

Park, J., Do, S., Lee, M., Ha, S., & Lee, K.-G. (2022). Preparation of Turmeric Powder with Various Extraction and Drying Methods. *Chemical and Biological Technologies in Agriculture*, *9*(39), 1–9. https://doi.org/10.1186/s40538-022-00307-1

Parunyakul, K., Srisuksai, K., Santativongchai, P., Pongchairerk, U., Ampawong, S., Tulayakul, P., & Fungfuang, W. (2022). The First Study on the Effect of Crocodile Oil from Crocodylus siamensis on Hepatic Mitochondrial Function for Energy Homeostasis in Rats. *Veterinary World*, *15*(4), 986–997. https://doi.org/10.14202/vetworld.2022.986-997

Ramírez-Moreno, E., Arias-Rico, J., Jiménez-Sánchez, R. C., Estrada-Luna, D., Jiménez-Osorio, A. S., Zafra-Rojas, Q. Y., Ariza-Ortega, J. A., Flores-Chávez, O. R., Morales-Castillejos, L., & Sandoval-Gallegos, E. M. (2022). Role of Bioactive Compounds in Obesity : Metabolic Mechanism Focused on Inflammation. *Foods*, *11*(1232), 1–23. https://doi.org/10.3390/foods11091232

Reski, S., Mundhofir, F. E. P., Murbawani, E. A., Nindita, Y., Muniroh, M., Swastawati, F., & Mahati, E. (2021). Efficacy of Catfish (Pangasius Hypophthalmus) Oil to Overcome Stunting by Reducing Inflammatory Condition. *International Journal of Pharmacy and Pharmaceutical Sciences*, *13*(5), 18–22. https://doi.org/10.22159/ijpps.2021v13i5.40357

Rezki, R. S., Anggoro, D., & Mz, S. (2015). Ekstraksi Multi Tahap Kurkumin dari Kunyit (Curcuma domestica Valet) Menggunakan Pelarut Etanol. *Jurnal Teknik Kimia USU*, *4*(3), 29–34. https://doi.org/10.32734/jtk.v4i3.1478

Rochlani, Y., Pothineni, N. V., Kovelamudi, S., & Mehta, J. L. (2017). Metabolic Syndrome: Pathophysiology, Management, and Modulation by Natural Compounds. *Therapeutic Advances in Cardiovascular Disease*, *11*(8), 215–225. https://doi.org/10.1177/1753944717711379

Sá, R. D. C. da C. de., Cruz, M. M., Farias, T. M. de., Silva, V. S. da., Simão, J. de J., Telles, M. M., & Alonso-Vale, M. I. C. (2020). Fish Oil Reverses Metabolic Syndrome, Adipocyte Dysfunction, and Altered Adipokines Secretion Triggered by High-Fat Diet-Induced Obesity. *Physiological Reports*, *8*(e14380), 1–13. https://doi.org/10.14814/phy2.14380

Saklayen, M. G. (2018). The Global Epidemic of the Metabolic Syndrome. *Current Hypertension Reports*, *20*(12), 1–8. https://doi.org/10.1007/s11906-018-0812-z

Sari, R. N., Utomo, B. S. B., Basmal, J., & Hastarini, E. (2016). Pemurnian Minyak Ikan Patin dari Hasil Samping Pengasapan Ikan. *Jurnal Pascapanen dan Bioteknologi Kelautan dan Perikanan*, *11*(2), 171–182. https://doi.org/10.15578/jpbkp.v11i2.224

Sasanfar, B., Toorang, F., & Salehi-Abarghouei, A. (2024). Effects of n-3 Polyunsaturated Fatty Acid Supplementation on Appetite: A Systematic Review and Meta-Analysis of Controlled Clinical Trials. *Systematic Reviews*, *13*(44), 1–11. https://doi.org/10.1186/s13643-023-02430-y

Sembiring, L., Ilza, M., & Diharmi, A. (2018). Karateristik Minyak Murni dari Lemak Perut Ikan Patin (Pangasius hypophthalmus) dan Dipurifikasi dengan Bentonite. *Jurnal Pengolahan Hasil Perikanan Indonesia*, *21*(3), 549–555. Retrieved from https://journal.ipb.ac.id/index.php/jphpi/article/download/24742/16119/

Shahidi, F., & Ambigaipalan, P. (2018). Omega-3 Polyunsaturated Fatty Acids and Their Health Benefits. *Annual Review OfFood Science and Technology*, *9*, 345–381. https://doi.org/10.1146/annurev-food-111317-095850

Shehadeh, M. B., Suaifan, G. A. R. Y., & Abu-Odeh, A. M. (2021). Plants Secondary Metabolites as Blood Glucose- Lowering Molecules. *Molecules*, *26*(4333), 1–46. https://doi.org/10.3390/molecules26144333

Sokamte, T. A., Mbougueng, P. D., Mohammadou, B. A., Tatsadjieu, N. L., & Sachindra, N. M. (2020). Proximal Composition and Fatty Acid Profile of Fresh and Smoked Fillets of Pangasius hypophthalmus. *Scientific African*, *9*(e00534), 1–9. https://doi.org/10.1016/j.sciaf.2020.e00534

Spencer, M., Finlin, B. S., Unal, R., Zhu, B., Morris, A. J., Shipp, L. R., Lee, J., Walton, R. G., Adu, A., Erfani, R., Campbell, M., Jr, R. E. M., Peterson, C. A., & Kern, P. A. (2013). Omega-3 Fatty Acids Reduce Adipose Tissue Macrophages in Human Subjects With Insulin Resistance. *Diabetes*, *62*, 1709–1717. https://doi.org/10.2337/db12-1042

Suaifan, G. A. R. Y., Shehadeh, M. B., Darwish, R. M., Al-ijel, H., & Abbate, V. (2015). Design, Synthesis and in Vivo Evaluation of Novel Glycosylated Sulfonylureas as Antihyperglycemic Agents. *Molecules*, *20*, 20063–20078. https://doi.org/10.3390/molecules201119676

Sulistyaningrum, H., Swastawati, F., Mexitalia, M., & Noer, E. R. (2021). Catfish Oil (Pangasius hypophthalmus) Effect to Ferritin and sTfR in Iron Deficiency Anemia. *Jurnal Gizi Indonesia (The Indonesian Journal of Nutrition)*, *10*(1), 28–35. https://doi.org/10.14710/jgi.10.1.28-35

Suryawanshi, H., Naik, R., Kumar, P., & Gupta, R. (2017). Curcuma Longa Extract – Haldi: A Safe, Eco-Friendly Natural Cytoplasmic Stain. *Journal of Oral and Maxillofacial Pathology*, *21*(3), 340–344. https://doi.org/10.4103/jomfp.JOMFP_62_17

Suseno, S. H., Rizkon, A. K., Jacoeb, A. M., Nurjanah, N., & Supinah, P. (2020). Ekstraksi Dry Rendering dan Karakterisasi Minyak Ikan Patin (Pangasius sp.) Hasil Samping Industri Filet di Lampung. *Jurnal Pengolahan Hasil Perikanan Indonesia*, *23*(1), 38–46. https://doi.org/10.17844/jphpi.v23i1.30722

Tanvir, E. M., Hossen, S., Hossain, F., Afroz, R., Gan, S. H., Khalil, I., & Karim, N. (2017). Antioxidant Properties of Popular Turmeric (Curcuma longa) Varieties from Bangladesh. *Journal of Food Quality*, 1–9. https://doi.org/10.1155/2017/8471785

Tortosa-caparrós, E., Navas-carrillo, D., Marín, F., & Orenes-piñero, E. (2016). Anti-Inflammatory Effects of Omega 3 and Omega 6 Polyunsaturated Fatty Acids in Cardiovascular Disease and Metabolic Syndrome. *Critical Reviews in Food Science and Nutrition*, *57*(16), 3421–3429. https://doi.org/10.1080/10408398.2015.1126549

U.S. Department of Health and Human Services & U.S. Department of Agriculture. (2015). *Dietary Guidelines For Americans 2015-2020* (8th ed.). Retrieved from https://health.gov/our-work/food-nutrition/previous-dietary-guidelines/2015

Uchio, R., Muroyama, K., Okuda-Hanafusa, C., Kawasaki, K., Yamamoto, Y., & Murosaki, S. (2019). Hot Water Extract of Curcuma longa L. Improves Serum Inflammatory Markers and General Health in Subjects with Overweight or Prehypertension/Mild Hypertension: A Randomized, Double-Blind, Placebo-Controlled Trial. *Nutrients*, *11*(1822), 1–17. https://doi.org/10.3390/nu11081822

Uchio, R., Okuda-Hanafusa, C., Saji, R., Kawasaki, K., Muroyama, K., Murosaki, S., Yamamoto, Y., & Hirose, Y. (2022). A Hot Water Extract of Curcuma longa L. Improves Fasting Serum Glucose Levels in Participants with Low-Grade Inflammation: Reanalysis of Data from Two Randomized, Double-Blind, Placebo-Controlled Trials. *Nutrients*, *14*(18). https://doi.org/10.3390/nu14183763

Venkateshwari, T., Ganapathy, S., Arulmari, R., & Vijayakumary, P. (2021). Effect of Drying Temperature on the Curcumin Content of Turmeric Rhizomes (Curcuma longa L.). *The Pharma Innovation Journal*, *10*(10), 2349–2351.

Retrieved from http://www.thepharmajournal.com

Xu, F., Fan, W., Wang, W., Tang, W., Yang, F., Zhang, Y., Cai, J., Song, L., & Zhang, C. (2018a). Effects of Omega-3 Fatty Acids on Metabolic Syndrome in Patients with Schizophrenia : A 12-Week Randomized Placebo-Controlled Trial. *Psychopharmacology*, *236*, 1273–1279. https://doi.org/10.1007/s00213-018-5136-9

Xu, L., Li, Y., Dai, Y., & Peng, J. (2018b). Natural Products for the Treatment of Type 2 Diabetes Mellitus: Pharmacology and Mechanisms. *Pharmacological Research*, *130*, 451-465. https://doi.org/10.1016/j.phrs.2018.01.015

Yi, T., Li, S. M., Fan, J. Y., Fan, L. L., Zhang, Z. F., Luo, P., Zhang, X. J., Wang, J. G., Zhu, L., Zhao, Z. Z., & Chen, H. B. (2014). Comparative Analysis of EPA and DHA in Fish Oil Nutritional Capsules by GC-MS. *Lipids in Health and Disease*, *13*(190), 1–6. https://doi.org/10.1186/1476-511X-13-190