Systematic Review: Phytochemical Content and Pharmacological Effects of *Chrysanthemum Sp.*

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Abstract

Chrysanthemum sp is a plant that is often used by the community as an ornamental plant, drink and traditional medicine. This study aims to examine the plant *Chrysanthemum sp* from the aspect of phytochemical and pharmacological activity. The review method used in this study is the PRISMA method. Sources of data obtained using *databases* electronic from *PubMed* and *Google Scholar*. The results of this review show that plants *Chrysanthemum sp* have phytochemical and pharmacological potential. The compounds contained in the plant *Chrysanthemum sp* are morphine, *genistein*, *hydantoin*, limonene, g-terpinene, a-pinene, a-terpenyl acetate, 4-terpenyl acetate, a-calacorene, a-cedrene, b-bourbobene, elemol, 2-hexenal, and *orphenadrine*. Chrysanthemum plants have anticancer, antibacterial, antioxidant, antifungal, analgesic, anti-inflammatory and anticonsulvan activities.

***Key words**: Chrysanthemum sp, pharmacological activity, phytochemic*

Introduction

Chrysanthemum sp is a type of plant that is in great demand by the public and is often used as an ornamental plant. A part from being an ornamental plant, chrysanthemum also has the potential as a medicinal plant. The group of chemical compounds contained in chrysanthemum plants are flavonoids, alkaloids, tannins, and terpenoids (Jung, EK 2009).

Previous literature mentions that the plant *Chrysanthemum sp* contains phytochemicals that have potential as drugs. These phytochemicals are reported to have antiallergic, antioxidant, and antimicrobial activity (Yang et al. 2017). However, in the previous literature review, comprehensive data on the phytochemical content, pharmacological effects and mechanism of action have not been presented. The purpose of this research is to examine the phytochemical aspects and

pharmacological activities as well as the mechanism of action of the plant *Chrysanthemum sp* . of various species.

Method

The method used in this study is a *systematic review in* accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA). Sources of data were obtained from *the database* electronic *PubMed*, and *Google Scholar*. The keywords used are *chrysanthemum, activity, secondary metabolites* and *chemical composition*. The inclusion criteria used were articles from 2009-2021, using English and Indonesian. The type of article used is Original Article and the content of the manuscript that is relevant to the specified topic. Meanwhile, the research exclusion criteria were articles published before 2009 and *Review Articles*.

The search resulted in 209 articles which were then filtered according to the subject of the desired material, namely the phytochemical content and pharmacological effects of the plant *Chrysanthemum sp* so that 5 articles were selected for review. Furthermore, a comparison and analysis of the articles that have been obtained is carried out to be developed into a review article.

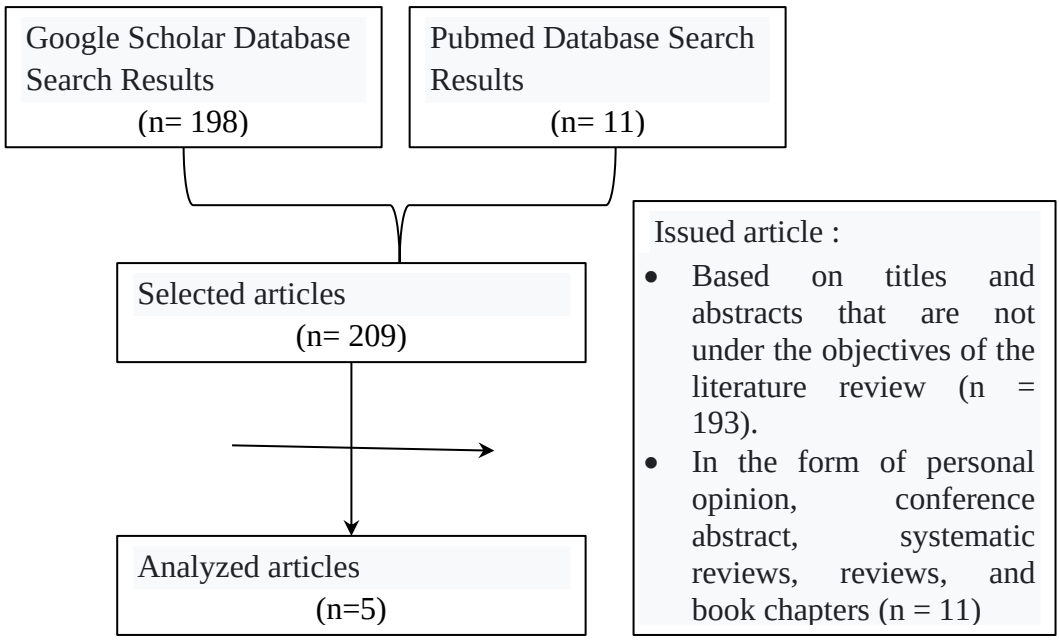

Figure 1. Diagram of PRISMA *Guideline systematic review of* plants *Chrysanthemum sp.*

Taxonomy

Chrysanthemum sp is a plant that belongs to the division *Spermatophyta* with sub-division *Angiospermae*. *Chrysanthemum sp* belongs to the class *Dycotiledonae*, order Asterales, family Asteraceae, and genus *Chrysanthemum*. *Chrysanthemum sp* has several species including *Chrysanthemum morifolium, Chrysanthemum maximum, Chrysanthemum daisy, Chrysanthemum indicum, and Chrysanthemum parthenium* (Tjitrosoepomo, 2013).

Botanical description

Plants *Chrysanthemum sp* has a white taproot. Stem height ranges from 0.5-1 m. The stem of *Chrysanthemum sp* is green, round, erect, and slightly branched, and has a rough surface (Andiani, 2013). Leaf *Chrysanthemumsp* is a type of single alternate leaves with pointed tip, base rounded shape, and has a bertoreh edge.leaves *Chrysanthemum sp.* green and has a rough surface.leaf size *Chrysanthemum sp* . ranging from 7-13 cm for leaf length, and 3-6 cm for leaf width (Andiani, 2013). Flower *Chrysanthemumsp* including compound interest form, which has a diameter of 3-5 cm.flower petals *Chrysanthemum sp* . cup-shaped, pointed tip, and has stamens and a fine pistil located in the middle of the flower, (Andiani, 2013).

(A) (B) (C) (D)

Figure 2. (a) The roots of Chrysanthemum, (B) Rod Chrysanthemum, (C) leaves Chrysanthemum, and D (Chrysanthemum)

Distribution of Geographic

*Chrysanthemum s*p found in Indonesia, Malaysia, China, Singapore, Australia, China, the Netherlands, Brunei, and Vietnam (Ekanantari, 2014). There are about 40 species of chrysanthemum scattered in Asia and Eastern Europe (Ryu, 2019).

Traditional Uses

Chrysanthemum sp is often used as a traditional medicine by the community. Dosage forms that are often made such as herbal drinks in the form of tea are believed to be able to treat health problems that occur in the community such as diseases caused by bacteria (Setiawati, 2019). In traditional Chinese medicine, chrysanthemum is used as an anti-inflammatory (Yang et al. 2017).

Active Compound

Extraction of essential oils in *Chrysanthemum sp*. So far it was reported that the main compounds in the leaves were limonene (26.83%), g-terpinene (19.68%), a-pinene (9.7%) and a-terpenyl acetate (7.16%). While in the stem it contains limonene (32.91%), 4-terpenyl acetate (16.33%) and g-terpinene (5.93%), while in the roots is a compound a-calacorene (25.98%), a-cedrene (16.55%), b-bourbobene (14.91%), elemol (7.45%) and 2-hexenal (6.88%) (Sassi, et al, 2014).

Metabolite profiles performed using UPLC-QToF-MS/MS showed differences in metabolite profiles in roots, stems, leaves, and chrysanthemums. Typical compounds in the flower parts are morphine and in the leaves genistein and ethanolamine. The main compound in roots, stems, and leaves was Orphenadrine with a percentage of 9.11%, 10.16%, and 3.24%, respectively, and the main compound in the flower part was Morphine with a percentage of 10.86% (Listiyana, et al. al, 2019).

Results and Discussion

Based on the results of the article search, the authors found 5 articles that matched the topic to be reviewed. A summary of the articles is presented in table 1.

Table 1. Table of active compounds isolated from *Chrysanthemum sp.* and pharmacological activity.

Types of Plants	Active Compounds	Pharmacological Activity	Reference
Chrysanthemum cinerariifolium	Orphenadrine	Anticancer	Listiyana, et al (2019)-terpinene, -pinene, -pinene
Chrysanthemum trifurcatum	*Limonene,and 4-terpenyl acetate.*	Antibacterial	Sassi, et al (2014)
sp Crhysanthemum	Flavonoids	Antioxidant	Yulianti, et al (2019)
Chrysanthemum morifolium	zingiberene, ® -sesquiphellandrene, α-curcumene, (E) -®-farnesene, α-farnesene, dan1,8-cineole	Antifungal	Xue, et al (2019)
Chrysanthemum trifurcatum	alkaloids and flavonoids	Analgesics	Salem, et al (2019)
Chrysanthemum trifurcatum	flavonoids	Anti-inflammatory	Salem, et al (2019)
Chrysanthemum trifurcatum	hydantoin	Antikonsulvan	Salem, et al (2019)

Bioactivity

Scientific evidence *Chrysanthemum sp*. Several pharmacological activities have been reported, namely, anticancer, antimicrobial, antioxidant, antifungal, analgesic, anti-inflammatory, and anticonvulsant. Each pharmacological activity and its mechanism are described as follows:

Anticancer Activity

Extracts of flowers, leaves, stems, and roots of *Chrysanthemum sp is* reported to have different chemical contents. These differences caused differences in cytotoxic activity in T47D cells. It is known that the *lead compound* from this plant is orphenadrine. There is a relationship between anticancer cytotoxic activity andlevels *orphenadrine* in each part of *Chrysanthemum sp*. The higher the levels ofcompounds *orphenadrine* in plants, the higher the anticancer potential (Listiyana, et al, 2019). Mechanism of *orphenadrine* in *Chrysanthemum sp* as an anticancer is to inhibit the work of cyclin dependent kinase (CDK) which is a cell cycle regulator through *activating kinase*, so that it can inhibit the formation of an active CDK-Cyclin complex (Mutiah et al, 2020).

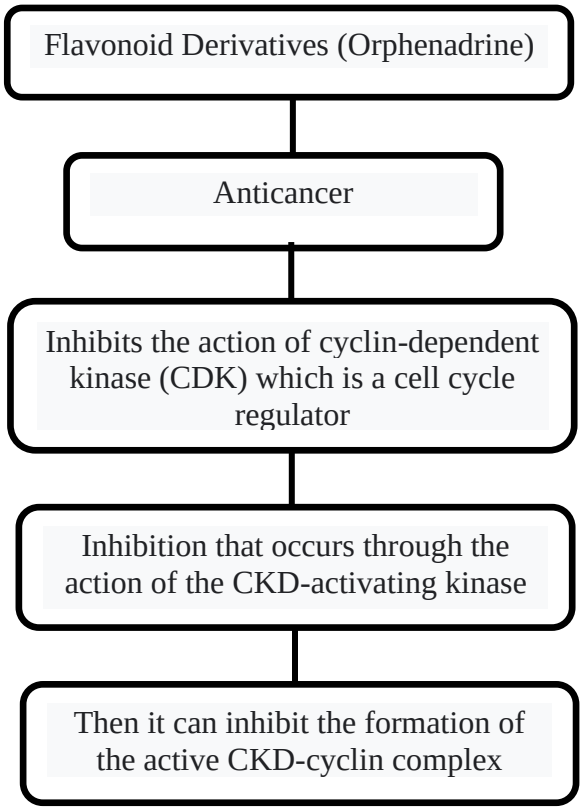

Figure 3. Mechanism of action of flavonoid derivatives as anticancer (Mutiah et al, 2020).

Antibacterial Activity

Essential oil fromleaves *Chrysanthemum sp*. showed antibacterial effect against *Bacillus subtilis* and *Staphylococcus epidermidis*, with anrange of IC_{50} 31.25-62.5 g/ml (Sassi, *et al.*, 2014). The mechanism of action of monoterpenes as antibacterial is by diffusion into cells and damaging the structure of cell membranes (Sassi, et al, 2014).

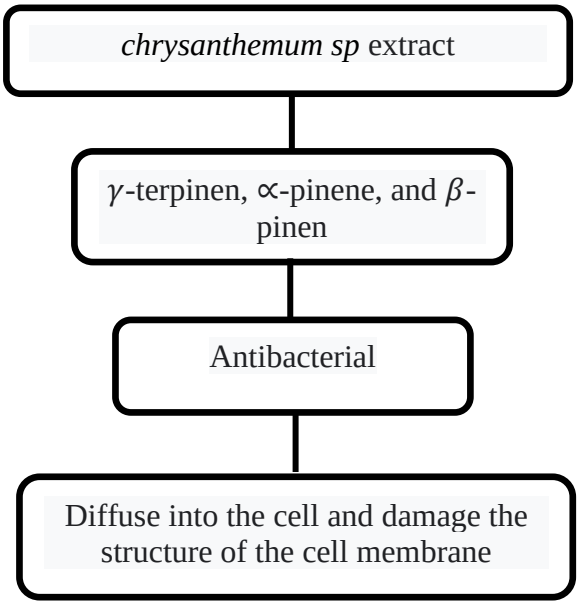

Figure 4. The mechanism of action of Monoterpenes as antibacterial on *Chrysanthemum sp* (Sassi, et al, 2014).

Antioxidant activity

Of chrysanthemum leaf simplicia was reported to have antioxidant activity with an ICvalue of$_{50}$ 139.19 ppm. The IC$_{50\ value}$ which is in the range of 50-200 ppm indicates the intensity as a strong antioxidant in chrysanthemum simplicia (Yulianti, 2019). The mechanism of action as an antioxidant is by donating hydrogen ions and then neutralizing the toxic effects of free radicals.

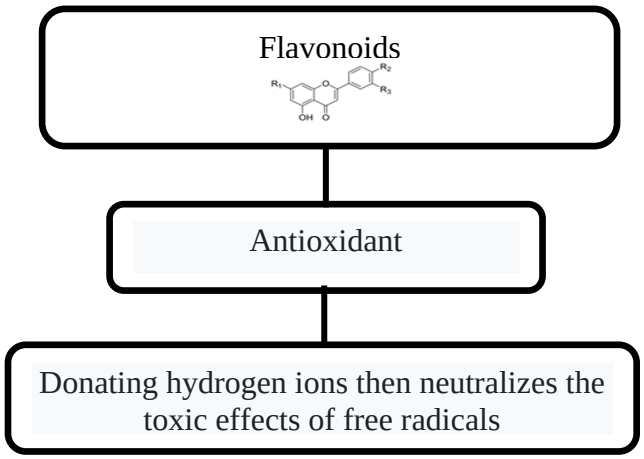

Figure 5. The mechanism of action of flavonoids as antibacterial in *Chrysanthemum sp*

Antifungal Activity

The results collectively indicate that the antifungal properties of secondary metabolites leaves of *C. morifolium* partly be attributed to the content of some terpenoids, including zingiberene, ®-sesquiphellandrene, α-curcumene, (E) -®-farnesene, α-farnesene, and 1,8-cineole (Xue, et al, 2019). The mechanism of terpenoid derivatives in *Chrysanthemum sp* as an antifungal is by reducing the permeability of the cell membrane of microorganisms. Then it binds with protein and lipid molecules so that it affects the physiological function of cell membrane proteins and enzyme proteins (Komala, et al, 2019).

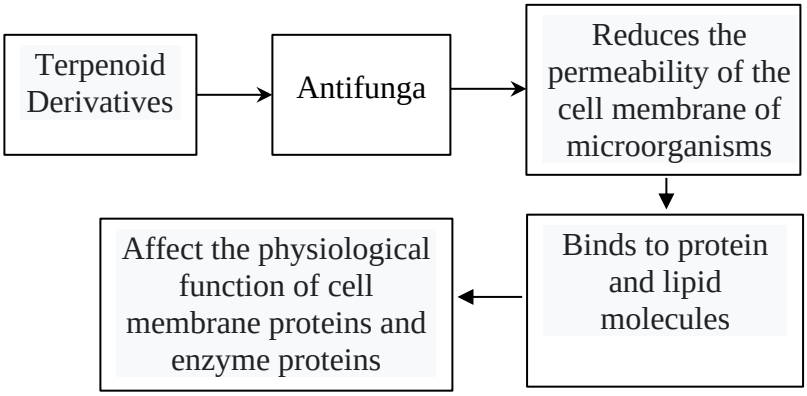

Figure 6. Mechanism of action of terpenoid derivatives as antifungal *Chrysanthemum sp* (Komala, et al, 2019).

Analgesic activity

The analgesic effect of *Chrysanthemum sp.* has been reported using a pain model method involving peripheral and central mechanisms with acetic acid induction in experimental animals. extract *Chrysanthemum trifurcatum* (300 mg/kg) exhibited an analgesic effect with approximately 64% significant inhibition. The analgesic activity of extract is *Chrysanthemum trifurcatum* due to the presence of alkaloids and flavonoids in the extract *Chrysanthemum trifurcatum* (Salem, et al, 2019). The mechanism of action of alkaloids and flavonoids as analgesics is by inhibiting the cyclooxygenase and 5-lipoxygenase pathways so that arachidonic acid synthesis decreases (Salem, et al, 2019).

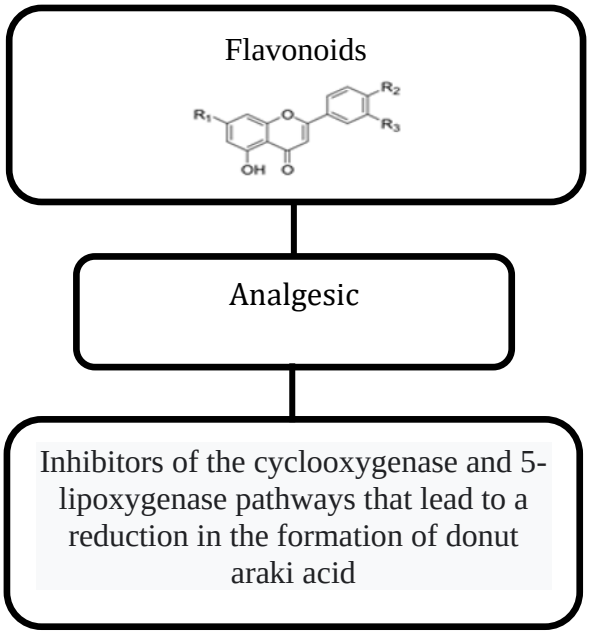

Figure 7. The mechanism of action of flavonoids as analgesics in *Chrysanthemum sp* (Salem, et al, 2019).

***Anti*-inflammatory**

Inflammatory activity The anti-inflammatory activity ofextract *Chrysanthemum trifurcatum* was evaluated by the percent inhibition of edema reduction performed in carrageenan-induced rats. Several comparisons between the tested groups revealed that oral administration ofextract *Chrysanthemum trifurcatum* at doses of 300 and 500 mg/kg showed a reduction in edema.extract *Chrysanthemum trifurcatum* at a dose of 300 mg/kg caused a significant reduction in leg edema at 5 hours post-administration. Meanwhile,extract *Chrysanthemum trifurcatum* at a dose of 500 mg/kg reduced leg edema at all test time points (Salem, et al, 2019). The mechanism of action of flavonoids inextract *Chrysanthemum trifurcatum* as an anti-inflammatory is to inhibit the formation of prostaglandins and cyclooxygenase (Salem, et al, 2019).

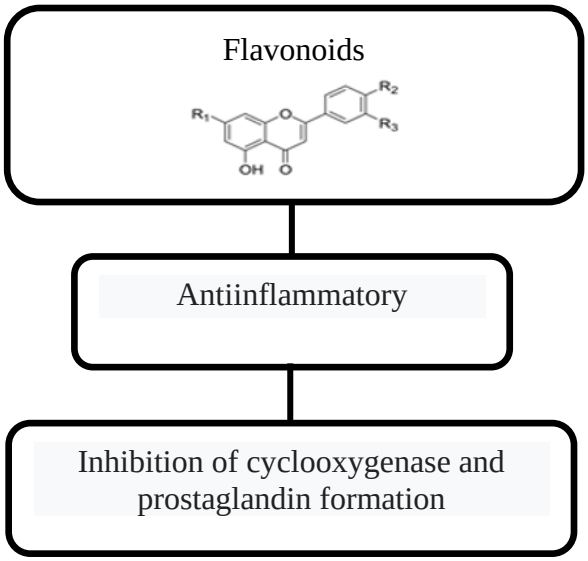

Figure 8. Mechanism of action of flavonoids as anti-inflammatory in *Chrysanthemum* (Salem, et al, 2019).

Anticonsulvan activity

Extract *Chrysanthemum trifurcatum* given to rats after being induced by Pentylenetetrazole revealed thatextract *Chrysanthemum trifurcatum* at a dose of 300 mg/kg had anticonsulvan activity.extract *Chrysanthemum trifurcatum* provided significant variation in latency time for clonic seizures (6.60 ± 0.67) and tonic seizures (9.92 ± 0.97). In addition,Extract *Chrysanthemum trifurcatum* significantly reduced mortality by 50% compared to 100% mortality in the control group (Salem, et al, 2019). The mechanism of action of hydantoin in *Chrysanthemum trifurcatum* as an anticonsulvan is to delay seizure induction by stimulating the GABA neurotransmitter so that it becomes active (Salem, et al, 2019).

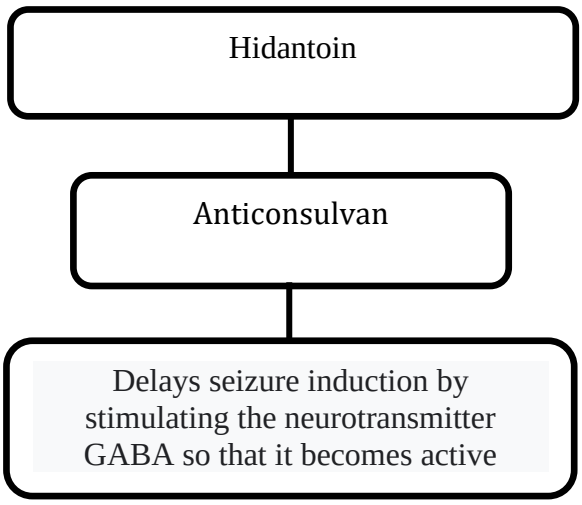

Figure 9. Mechanism of action of hydantoin as an anticonsulvan (Salem, et al, 2019).

Conclusions

Plant *Chrysanthemum sp* has proven to have the potential chemical and pharmacological activity. The compounds contained in theplant *Chrysanthemum sp* are morphine, *genistein*, *hydantoin*, limonene, g-terpinene, a-pinene, a-terpenyl acetate, 4-terpenyl acetate, a-calacorene, a-cedrene, b-bourbobene, elemol, 2- hexenal, *ethanolamine*, a-terpenyl acetate and *orphenadrine*. The pharmacological activities of *Chrysanthemum sp* are anticancer, antibacterial, antioxidant, antifungal, analgesic, anti-inflammatory and anticonsulvan activities. Therefore, *Chrysanthemum sp* can be recommended as a candidate for herbal medicine. Based on the literature review, it can be concluded that compounds that have antibacterial activity are *limonene, -terpinene, -pinene, -pinene and 4-terpenyl acetate.* Compounds that have that have antifungal activity is zingiberene, ®-sesquiphellandrene, α-curcumene, (E)-®-farnesene, α-farnesene, and 1,8-cineole. Compounds that have anticonsulvan activity are hydantoins. The flavonoids and alkaloids have anti-inflammatory, analgesic, and antioxidant activities.

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References

Andiani, Yuli. (2013). *Budidaya Bunga Krisan*. Yogyakarta: Pustaka Baru Press.

Ekanantari. (2014). *Outlook komoditi krisan.* Jakarta: Pusat Data dan Sistem Informasi Pertanian.

Jung, E.-K. (2009). Chemical Composition and Antimicrobial Activity of the Essential Oil of *Chrysanthemum Indicum* Against Oral Bacteria. *J Bacteriol Virol* , 39 (2)

Komala, O., & Siwi, F. R. (2020). Aktivitas Antijamur Ekstrak Etanol 50% Dan Etanol 96% Daun Pacar Kuku *Lawsonia inermis* L terhadap *Trichophyton mentagrophyte*s. *EKOLOGIA*. 19(1), 12-19.

Listiyana, A., Lestari, N. A., Irawati, S., Indrawijaya, Y. Y. A., Annisa, R., Bhagawan, W. S.. & Ma'arif, B. (2019). Anticancer Activities and Metabolite Fingerprinting of UPLC-QTOF-MS/MS Method From *Chrysanthemum cinerariifolium* (Trev). *Journal of Islamic Pharmacy*, 4(1), 19-39.

Mutiah, R., Inayatin, A. L., Annisa, R., Indrawijaya, Y. Y. A., & Listiyana, A. (2020). Inhibition of Cell Cycle and Induction of Apoptosis y Ethanol Leaves Extract of *Chrysanthemum cinerariifolium* (Trev.) In T47D Breast Cancer Cells. Indonesian *Journal of Phar*macy. 31(1), 1.

Ryu, Jaihyunk, dkk. (2019). Comparative Analysis of Phytochemical Composition of Gamma-Irradiated Mutant Cultivars of *Chrysanthemum morifolium*. *Molecules*

Salem, G. A., Alamyel, F. B., Abushaala, F. A., Hussain, M. S., Abusheba, H., & Sahu, R. P. (2019). Evaluation of the hepatoprotective, anti-inflammatory, antinociceptive and antiepileptic activities of Chrysanthemum trifurcatum. *Biomedicine & Pharmacotherapy*. 117, 109123.

Sassi, A. B., Skhiri, F. H., Chraief, I., Bourgougnon, N., Hammami, M., & Aouni, M. (2014). Essential oils and crude extracts from *Chrysanthemum trifurcatum* leaves, stems and roots: chemical composition and antibacterial activity. *Journal of oleo science*, 63(6), 607-617.

Setiawati, Tia, dkk. (2019). Pengenalan Khasiat Obat Tanaman Krisan dan Pembuatan Teh Krisan Sebagai Minuman Kesehatan. *Jurnal Penelitian dan Pengabdian Masyarakat*. Vol 7, No 1.

Tjitrosoepomo G. (2013). *Taksonomi (Spermatophyta)*. Yogyakarta: Gajah Mada University Press.

Xue, H., Jiang, Y., Zhao, H., Köllner, T. G., Chen, S., Chen, F., & Chen, F. (2019). Characterization of composition and antifungal properties of leaf secondary metabolites from thirteen cultivars of *Chrysanthemum morifolium* Ramat. *Molecules*. 24(23), 4202.

Yang L, Aobulikasimu N, Ping C, Jin HW, Hong L. (2017). Analysis of Floral Volatile Components and Antioxidant Activity of Different Varieties of *Chrysanthemum morifolium. Molecules*

Yulianti, Dini, dkk. (2019). Aktivitas Antioksidan Daun Pegagan (*Centella Asiatica* L.Urban) Dan Bunga Krisan (*Crhysanthemum Sp*) Pada Tiga Variasi Suhu Pengeringan. *Pasundan Food Technology Journal*. Vol 6, No 3