

**PENGARUH PEMBERIAN KOMBUCHA DAUN
SIRSAK TERHADAP KERUSAKAN JARINGAN
RETINA IKAN ZEBRA (*Danio rerio*) YANG
DIINDUKSI SUKROSA 4%**

SKIRPSI

**Untuk Memenuhi Persyaratan
Memperoleh Gelar Sarjana Kedokteran**



Oleh

**Atikah Qotrul Himma
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**PROGRAM STUDI KEDOKTERAN
FAKULTAS KEDOKTERAN
UNIVERSITAS ISLAM MALANG
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RINGKASAN

Atikah Qotrul Himma, Fakultas Kedokteran, Universitas Islam Malang, Juni 2025. Pengaruh Pemberian Kombucha Daun Sirsak Terhadap Kerusakan Jaringan Retina Ikan Zebra (*Danio rerio*) yang Diiinduksi Sukrosa 4%. Pembimbing 1 : Dr. dr. Dini Sri Damayanti, M.Kes, Pembimbing 2 : dr. Aris Rosidah, M.Biomed., Sp. PA.

Pendahuluan : Hiperglikemia merupakan kondisi medis di mana kadar glukosa darah, dalam keadaan puasa >126 mg/dL. Peradangan yang berlangsung terus-menerus selama hiperglikemia akan meningkatkan kerusakan jaringan termasuk di retina mata. Daun sirsak salah satu tumbuhan herbal dengan kandungan flavonoid dan tannin yang mampu menurunkan kadar glukosa dalam darah. Kombucha memiliki sifat antihiperglikemia melalui mekanisme seperti regulasi mikrobiota intestinal dan peningkatan sekresi hormon di gastrointestinal. Induksi sukrosa 4% pada ikan zebra menyebabkan peningkatan apoptosis sel ganglion retina serta penurunan ketebalan *Inner Plexiform Layer* (IPL). Berdasarkan hal tersebut, penelitian ini bertujuan menguji pengaruh pemberian kombucha daun sirsak terhadap kematian sel ganglion retina dan penurunan ketebalan IPL retina ikan zebra.

Metode : Penelitian ini menggunakan ikan zebra dewasa usia 3-4 bulan, yang dibagi menjadi lima kelompok : kontrol (KN), sukrosa 4% (KP), serta kombinasi sukrosa 4% dengan kombucha daun sirsak dosis 1,25% (KP1), 2,5% (KP2), dan 5% (KP3). Perlakuan diberikan selama 28 hari, dilanjutkan pembuatan preparat, dengan pewarnaan HE. Apoptosis sel ganglion dibuat dalam bentuk persentase dan ketebalan IPL diukur menggunakan *imageJ* dengan satuan μm . Data dianalisa dengan *One Way ANOVA*, dengan $p < 0,05$ sebagai batas signifikan.

Hasil : Jumlah apoptosis sel ganglion retina (KP) $163,20 \pm 37,19$ meningkat dibandingkan (KN) $33,80 \pm 5,54$ ($p=0,001$). Pada (KP1) $66,20 \pm 13,84$ jumlah apoptosis sel ganglion retina menurun dibandingkan KP ($p=0,001$). (KP2) $177,13 \pm 26$ dan (KP3) $180,80 \pm 34,04$ tidak ada beda dengan KP. Ketebalan IPL retina menurun pada (KP) $95,00 \pm 6,36$ dibanding (KN) $143,00 \pm 24,19$ dan (KP1) $124,00 \pm 9,00$ ($p=0,001$). Pada (KP2) $74,20 \pm 18,67$ dan (KP3) $73,00 \pm 6,63$ tidak beda signifikan dengan KP.

Kesimpulan : Kombucha daun sirsak dosis 1,25% menurunkan jumlah apoptosis sel ganglion retina dan mengurangi penurunan ketebalan IPL retina ikan zebra.

Kata kunci : Ikan zebra, kombucha daun sirsak, sukrosa, retina

SUMMARY

Atikah Qotrul Himma, Faculty of Medicine, Islamic University of Malang, June 2025. The Effect of Soursop Leaf Kombucha on Retinal Tissue Damage in Zebrafish (*Danio rerio*) Induced by 4% Sucrose, Supervisor 1: Dr. dr. Dini Sri Damayanti, M.Kes, Supervisor 2 : dr. Aris Rosidah, M.Biomed., Sp. PA.

Introduction : Hyperglycemia is a medical condition characterized by fasting blood glucose levels exceeding 126 mg/dL. Persistent inflammation during hyperglycemia can lead to tissue damage, including retina. Soursop leaves are herbal plants containing flavonoids and tannins that have the ability to lower blood glucose levels. Kombucha exhibits antihyperglycemic properties through mechanisms such as modulation of intestinal microbiota and enhanced secretion of gastrointestinal hormones. Induction of 4% sucrose in zebrafish increases ganglion cell apoptosis and reduces the thickness of the Inner Plexiform Layer (IPL) in retina. Based on this, the study aims to examine the effect of soursop leaf kombucha on retinal ganglion death cell and IPL thickness in zebrafish.

Method : This study used zebrafish aged 3-4 months, divided into five groups : control (KN), 4% sucrose (KP), 4% sucrose combined with soursop leaf kombucha at doses of 1,25% (KP1), 2,5% (KP2), 5% (KP3). The treatment was given for 28 days, followed by preparation using HE staining. Ganglion cell apoptosis was presented as percentage, and IPL thickness was measured using imageJ software with units of μm . Data were analyzed using One Way ANOVA with a significance level of $p < 0,05$.

Result : The number of apoptotic retinal ganglion cells in (KP) $163,20 \pm 37,19$ increased compared to (KN) $33,80 \pm 5,54$ ($P=0,001$). In (KP1) $66,20 \pm 13,84$, the number of apoptotic cells decreased significantly compared to KP ($p=0,001$). The (KP2) $177,13 \pm 26$ and (KP3) $180,80 \pm 34,04$ groups showed no significant difference from KP. The IPL thickness in (KP) $96,00 \pm 6,36$ decreased compared to (KN) $143,00 \pm 24,19$ and (KP1) $124,00 \pm 9,00$ ($p=0,001$). The (KP2) $74,20 \pm 18,67$ and (KP3) $73,00 \pm 6,63$ groups showed no significant difference from KP.

Conclusion : Soursop leaf kombucha at a dose of 1,25% reduced the number of apoptotic retinal ganglion cells and reduce the decrease in IPL thickness in zebrafish.

Keyword : Zebrafish, soursop leaf kombucha, sucrose, retina

BAB I PENDAHULUAN

1.1 Latar Belakang Penelitian

Hiperglikemia merupakan kondisi medis di mana kadar glukosa darah, dalam keadaan puasa >126 mg/dL, sering dikaitkan dengan beberapa penyakit, terutama diabetes melitus (Roden and Shulman, 2019). *International Federation Diabetes* (IDF) memperkirakan bahwa prevalensi Diabetes Melitus 2 (DM2) sebesar 10,5% pada tahun 2021, akan meningkat menjadi 11,3% pada tahun 2030, tingkat insiden dan mortalitas DM2 pada pria lebih tinggi daripada wanita (Harreiter & Kautzky-Willer, 2018; Cooppan, 2016). Dampak utama bagi penderita diabetes adalah komplikasi jangka panjang, komplikasi mikrovaskular yang sering terjadi salah satunya Diabetik Retinopati (DR) (Squire, 2009). Dengan bertambahnya jumlah penderita DM2, diperkirakan yang mengalami retinopati diabetik mencapai 191 juta pada tahun 2030. Dari 1.184 orang berusia > 30 tahun dengan DM 2, prevalensi diabetik retinopati mencapai 43,1% (Pepose et al., 2014).

Sukrosa adalah disakarida yang terdiri atas glukosa dan fruktosa, bentuk karbohidrat yang sering dikonsumsi dalam kehidupan sehari-hari, juga disebut sebagai gula pasir. Diet tinggi sukrosa dapat menyebabkan terjadinya peningkatan lipogenesis, penurunan aktivitas enzim glukokinase, dan gangguan sekresi GLP-1, hal ini lebih menyebabkan hiperglikemia dibandingkan konsumsi glukosa saja (Sakamoto et al. 2012; Wahyudiati, 2017). Hiperglikemia menyebabkan stres oksidatif dan peradangan, stres oksidatif terjadi karena kelebihan glukosa darah akan memicu produksi radikal bebas yang dapat merusak sel dan jaringan. Peradangan yang berlangsung terus-menerus juga meningkatkan kerusakan

jaringan melalui pelepasan sitokin proinflamasi, yang berakibat adanya pembentukan AGEs, serta meningkatnya VEGF. Kondisi ini dapat merusak retina mata sehingga menyebabkan pembekuan cairan, iskemia, dan pembentukan pembuluh darah baru yang rapuh hingga dapat menyebabkan kebutaan (Yang et al. 2024).

Di Indonesia, keberagaman sumber daya alam memudahkan akses ke berbagai jenis tanaman herbal. Hal ini menjadikan obat herbal sebagai pilihan terapi yang terjangkau dan berkelanjutan (Grenvilco DO. et al. 2023). Pencegahan penyakit degeneratif, termasuk DM 2 selain melalui perubahan gaya hidup juga dapat dibantu melalui konsumsi obat herbal. (Kooti et al., 2016). Daun sirsak salah satu tumbuhan herbal yang mengandung banyak fenol, termasuk senyawa seperti terpenoid, flavonoid, alkaloid, dan tanin (Ningsih, 2016). Kandungan flavonoid dan tanin dapat membuat kadar glukosa dalam darah turun (Sovia et al. 2017).

Kombucha merupakan herbal teh olahan yang kaya akan polifenol dan memiliki aktivitas antihiperglikemia. Kombucha mengandung probiotik, asam organik, dan senyawa fenolik. Konsumsi probiotik dapat meningkatkan pertahanan sistem imun non-spesifik. Kombucha memiliki sifat antihiperglikemia melalui beberapa mekanisme seperti regulasi mikrobiota intestinal, peningkatan sekresi hormon di gastrointestinal, pengurangan inflamasi, serta peningkatan sensitivitas insulin (Hrnjez et al. 2014; Xu et al. 2022). Kombucha dapat menurunkan hiperglikemia pada tikus setelah 4 minggu intervensi. Kadar glukosa darah puasa pada tikus menurun signifikan dibandingkan dengan kelompok kontrol tanpa perlakuan, penurunan kadar gula puasanya sekitar 15,22 mmol/L. Penelitian sebelumnya yang dilakukan pada manusia menunjukkan konsumsi kombucha

terbukti menurunkan kadar gula darah puasa pada pasien DM2. Rerata kadar glukosa darah puasa setelah 4 minggu konsumsi kombucha menurun signifikan, dari 164 mg/dl menjadi 116 mg/dl. Hasil ini menunjukkan potensi kombucha sebagai antihiperglikemia (Xu et al. 2022 dan Mendelson et al. 2023).

Penelitian menggunakan hewan coba ikan zebra digunakan karena memiliki sejumlah keunggulan untuk penelitian penyakit manusia, termasuk perkembangan yang cepat dan khususnya kesamaan gen 70% dengan manusia (Choi et al. 2021). Penelitian sebelumnya menunjukkan induksi hiperglikemia pada ikan zebra dilakukan dengan merendam dalam larutan sukrosa dengan konsentrasi 1%, 2%, dan 4% selama 28 hari. Penelitian lain mengungkapkan adanya peningkatan apoptosis sel ganglion retina serta penurunan ketebalan *Inner Plexiform Layer* (IPL) yang signifikan pada konsentrasi 4% (Fauziah, N. Et al. 2024). Berdasarkan hal tersebut, penelitian ini bertujuan menguji pengaruh pemberian kombucha daun sirih terhadap kematian sel ganglion retina dan penurunan ketebalan IPL retina ikan zebra yang diinduksi oleh sukrosa 4%.

1.2 Rumusan Masalah

1. Apakah pemberian kombucha daun sirih dapat menurunkan apoptosis sel ganglion retina pada ikan zebra yang telah diinduksi sukrosa 4%?
2. Apakah pemberian kombucha daun sirih dapat mencegah penurunan ketebalan IPL retina pada ikan zebra yang telah diinduksi sukrosa 4%?

1.3 Tujuan Penelitian

1. Mengetahui pengaruh pemberian kombucha daun sirih terhadap apoptosis sel ganglion retina pada ikan zebra yang telah diinduksi sukrosa 4%.

2. Mengetahui pengaruh pemberian kombucha daun sirsak terhadap penurunan ketebalan IPL retina pada ikan zebra yang telah diinduksi sukrosa 4%.

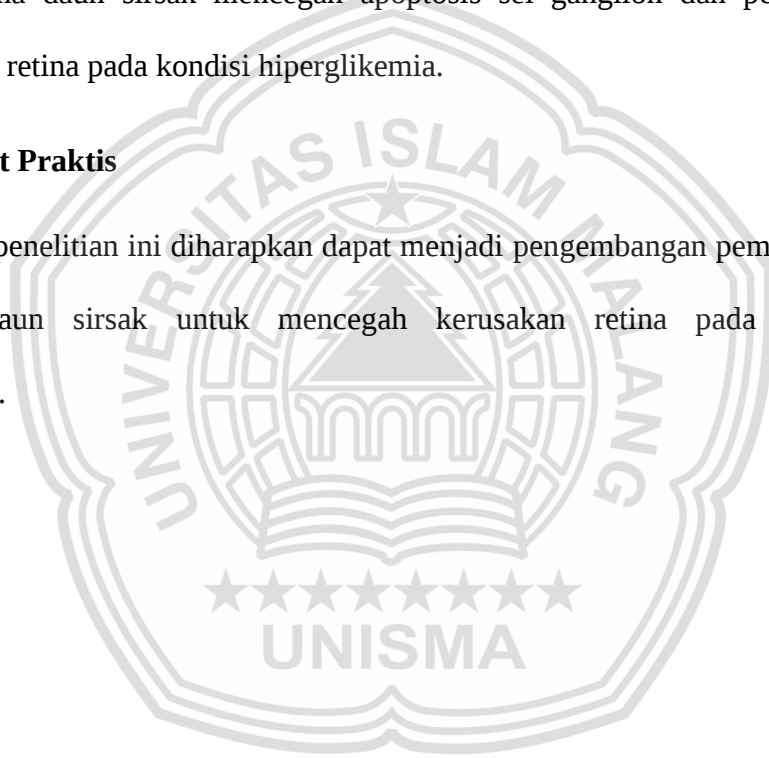
1.4 Manfaat Penelitian

1.4.1 Manfaat Teoritis

Penelitian ini diharapkan dapat dijadikan landasan teori untuk mengetahui efek kombucha daun sirsak mencegah apoptosis sel ganglion dan penurunan ketebalan IPL retina pada kondisi hiperglikemia.

1.4.2 Manfaat Praktis

Hasil penelitian ini diharapkan dapat menjadi pengembangan pemanfaatan kombucha daun sirsak untuk mencegah kerusakan retina pada kondisi hiperglikemia.



BAB VII

PENUTUP

7.1 Kesimpulan

Berdasarkan hasil Analisa data dan pembahasan yang telah dilaksanakan, dapat disimpulkan beberapa hal penting sebagai berikut :

1. Pemberian kombucha daun sirsak dosis 1,25% terbukti paling efektif dalam menurunkan jumlah apoptosis sel ganglion serta mengurangi penurunan ketebalan IPL retina ikan zebra.
2. Dosis 2,5% & 5% kombucha daun sirsak menunjukkan efek toksik, ditandai dengan peningkatan jumlah apoptosis sel ganglion retina serta penurunan ketebalan IPL.

7.2 Saran

Beberapa masukan dapat diberikan untuk pengembangan penelitian ini lebih lanjut sebagai berikut :

1. Menguji dosis dibawah 1,25% guna menentukan dosis optimal yang memiliki efek terapeutik tanpa menimbulkan toksisitas terhadap kerusakan retina.
2. Melakukan pengukuran panjang & berat badan setelah proses perlakuan sebagai indikator kesehatan serta mendeteksi kemungkinan adanya efek samping.
3. Sisa sampel ikan yang tidak digunakan sebaiknya dibentuk dalam parafin sebagai cadangan guna mengantisipasi kemungkinan tingginya simpangan baku pada data.

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