# PENGARUH PEMBERIAN SUKROSA KONSENTRASI 1%, 2%, DAN 4% TERHADAP KERUSAKAN SEL HEPAR PADA IKAN ZEBRA (*Danio rerio*)

## SKRIPSI

**Untuk Memenuhi Persyaratan**

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## RINGKASAN

**Tita Setia Wany**, Fakultas Kedokteran, Universitas Islam Malang, 2025. Pengaruh Pemberian Sukrosa Konsentrasi 1%, 2%, dan 4% Terhadap Kerusakan Sel Hepar Pada Ikan Zebra (*Danio rerio*). **Pembimbing 1**: Dr. dr. Dini Sri Damayanti, M.Kes, **Pembimbing 2**: dr. Hj. Noer Aini, M.Kes.

**Pendahuluan:** Konsumsi sukrosa berlebih dalam waktu lama dapat memicu hiperglikemia yang menyebabkan kerusakan hepar. Ikan zebra dipilih sebagai model hewan coba karena kesamaan genomnya dengan manusia dan kemiripan sistem organ.Penelitian ini bertujuan untuk membuktikan pengaruh pemberian sukrosa pada berbagai konsentrasi terhadap kerusakan hepar ikan zebra.

**Metode:** Penelitian secara eksperimental dengan menggunakan *posttest-only control design* pada ikan zebra. Kelompok penelitian terdiri dari tiga kelompok perlakuan dengan konsentrasi sukrosa 1%, 2%, dan 4%, serta satu kelompok kontrol tanpa pemberian sukrosa. Masing-masing kelompok terdiri dari 30 ekor ikan zebra. Diberikan selama 28 hari. Pembuatan preparat histologi hepar dengan pewarnaan hematoxylin-eosin (HE) dilakukan untuk mendeteksi adanya kerusakan hepatosit yaitu nekrosis inti hepatosit (piknosis, karioreksis, kariolisis, dan membrane lisis) serta steatosis hepatosit menggunakan mikroskop trinokuler dengan pembesaran 400x, 10 per lapang pandang dan 3 pengamat. Analisis data menggunakan uji Kruskal Wallis dan uji Mann-Whitney ($p<0.05$).

**Hasil:** Jumlah sel yang mengalami karioreksis pada kelompok 4% (327.5±4.45) berbeda secara signifikan dibandingkan kelompok normal (40.99±3.5), kelompok 1% (164.94±20.33), kelompok 2% (255.33±22.25). Begitupula pada variabel piknosis, kariolisis, dan membrane lisis. Jumlah sel yang mengalami steatosis pada kelompok 4% (347,83 ± 13,61) berbeda secara signifikan dibandingkan kelompok normal (104.95±0.13), kelompok 1% (144.56±2.29), dan kelompok 2% (279.11±7.98). Adanya peningkatan hepatosit yang mengalami nekrosis dan steatosis diduga disebabkan efek hiperglikemia akibat pemberian sukrosa. Hiperglikemia menyebabkan peningkatan produksi radikal bebas. Semakin tinggi konsentrasi sukrosa yang diberikan, semakin besar stress oksidatif yang terjadi, sehingga memicu kerusakan hepatosit.

**Kesimpulan:** Pemberian sukrosa selama 28 hari dengan konsentrasi 1%, 2%, dan 4% menyebabkan nekrosis inti hepatosit dan stetatosis hepatosit ikan zebra. Kerusakan sel hepar meningkat seiring dengan peningkatan konsentrasi sukrosa yang diberikan.

**Kata Kunci:** Hiperglikemia, sukrosa, nekrosis, steatosis, hepar, *Danio rerio*.

## SUMMARY

**Tita Setia Wany**, Faculty of Medicine, University of Islam Malang, 2025. The Effect of 1%, 2%, and 4% Sucrose Administration on Hepatic Cell Damage in Zebra Fish (*Danio rerio*). **Supervisor 1:** Dr. dr. Dini Sri Damayanti, M.Kes, **Supervisor 2:** dr. Hj. Noer Aini, M.Kes.

**Introduction**: Excessive consumption of sucrose over a long period can trigger hyperglycemia, leading to liver damage. Zebrafish were chosen as the experimental animal model due to their genomic similarity to humans and the resemblance of their organ systems. This study aims to demonstrate the effect of administering sucrose at various concentrations on liver damage in zebrafish.

**Methods**: Experimental research using a posttest-only control design on zebrafish. The research groups consisted of three treatment groups with sucrose concentrations of 1%, 2%, and 4%, and one control group without sucrose administration. Each group consists of 30 zebrafish. Given for 28 days. The preparation of histological liver specimens with hematoxylin-eosin (HE) staining was performed to detect hepatocyte damage, namely hepatocyte nuclear necrosis (pyknosis, karyorrhexis, karyolysis, and membrane lysis), as well as hepatocyte steatosis using a trinocular microscope with 400x magnification, 10 fields of view, and 3 observers. Data analysis used the Kruskal-Wallis test and the Mann-Whitney test ($p < 0.05$).

**Results**: The number of cells experiencing karyorexis in the 4% group (327.5±4.45) was significantly different compared to the normal group (40.99±3.5), the 1% group (164.94±20.33), and the 2% group (255.33±22.25). The same was observed for the variables of pyknosis, karyolysis, and membrane lysis. The number of cells experiencing steatosis in the 4% group (347.83±13.61) was significantly different compared to the normal group (104.95±0.13), the 1% group (144.56±2.29), and the 2% group (279.11±7.98). The increase in hepatocytes experiencing necrosis and steatosis is suspected to be caused by the hyperglycemic effect due to sucrose administration. Hyperglycemia leads to an increase in free radical production. The higher the concentration of sucrose administered, the greater the oxidative stress that occurs, thereby triggering hepatocyte damage.

**Conclusion**: Administration of sucrose for 28 days at concentrations of 1%, 2%, and 4% caused necrosis of hepatocyte nuclei and hepatocyte steatosis in zebrafish. Liver cell damage increased with the higher concentration of sucrose administered.

**Keywords**: Hyperglycemia, sucrose, necrosis, steatosis, liver, *Danio rerio*.

# BAB I
# PENDAHULUAN

## 1.1 Latar Belakang

Hiperglikemia merupakan peningkatan kadar glukosa dalam darah. Hiperglikemia dapat terjadi pada kondisi infeksi, stress, trauma, maupun penyakit metabolik lainnya (Mouri & Badireddy, 2025). Salah satu penyakit metabolik yang sangat erat kaitannya dengan hiperglikemia adalah diabetes mellitus. Diabetes adalah penyakit kronis yang terjadi ketika pankreas tidak memproduksi cukup insulin atau ketika tubuh tidak dapat menggunakan insulin yang dihasilkan secara efektif (WHO, 2023). Indonesia adalah salah satu dari negara yang termasuk dalam *International Diabetes Federation* (IDF). Dilaporkan 537 juta orang menderita diabetes di dunia, diperkirakan pada tahun 2045 jumlah penderita diabetes sebanyak 784 juta orang di dunia atau meningkat sekitar 46%. Angka kematian diabetes sangat tinggi, dilaporkan 6,7 juta kematian pada tahun 2021. Pada tahun 2021, penderita diabetes mellitus usia 20-70 tahun di Indonesia adalah sekitar 10,6%. Angka tersebut akan terus meningkat, diperkirakan pada tahun 2030 penderita diabetes di Indonesia meningkat 16% (*International Diabetes Federation*, 2021). Diabetes ditandai dengan tingginya kadar gula darah atau hiperglikemia (PERKENI, 2021).

Hiperglikemia menjadi awal dari ketidakmampuan sel-sel tubuh untuk merespon sepenuhnya terhadap insulin, kondisi ini disebut resistensi insulin, yang akan berakibat pada kerusakan hepar (Mohamed et al., 2016). Resistensi insulin dapat diakibatkan oleh diet tinggi kalori dengan *life style* yang buruk. Resistensi insulin yang berlanjut menyebabkan de novo lipogenesis di intrahepatik, peningkatan lipolysis dan produksi asam lemak bebas berlebihan. Asam lemak

bebas kemudian dilepaskan ke aliran darah dan akhirnya terakumulasi di hepar. Pada saat yang sama, jaringan adiposit melepaskan faktor proinflamasi *tumor necrosis factor-α* (TNF-α) dan hormon leptin yang meningkatkan stres oksidatif di mitokondria. Stres oksidatif mitokondria dan hiperglikemia menghasilkan radikal bebas yang menyebabkan peradangan yang kemudian dapat berlanjut pada keadaan steatosis dan nekrosis inti hepatosit (Mohamed et al., 2016). Namun perlu adanya penelitian lebih lanjut untuk membuktikan teori tersebut.

Penelitian untuk membuktikan adanya kerusakan hepar karena hiperglikemia dapat dilakukan pada *Danio rerio* sebagai *animal model* dikarenakan memiliki struktur genom yang mirip dengan manusia (70%), selain itu pemeliharaannya yang relatif mudah dan memiliki sistem saraf, kardiovaskuler dan sistem digestif yang mirip dengan mamalia. Penelitian sebelumnya telah berhasil menjadikan *Danio rerio* sebagai *animal model* hiperglikemia dengan menginduksi larutan sukrosa 2% dinaikan bertahap selama 2 bulan terus menerus dan diamati peningkatan kadar sukrosa darah yang meningkat dan menetap sampai 8 minggu (Zang et al., 2018).

Penelitian tersebut berfokus pada induksi ikan zebra menjadi hiperglikemia melalui induksi sukrosa eksternal dengan mengandalkan sistem peredaran darah tunggal pada ikan zebra. Pada saat ikan menyerap air beroksigen dan beberapa nutrisi melalui insang, kemudian akan dilanjutkan ke arteri utama ikan beredar keseluruh tubuh, setelah pertukaran gas di kapiler dan menuju vena, aliran darah akan memasuki jantung dan kembali ke luar tubuh ikan melalui insang. Namun perlu adanya penelitian lebih lanjut untuk mengembangkan penelitian tersebut terutama efek hiperglikemia pada organ, khususnya hepar. Berdasarkan latar belakang di atas maka dilakukan penelitian untuk mengetahui efek pemberian

sukrosa dengan konsentrasi 1%, 2%, 4% pada *Danio rerio* terhadap kerusakan organ hepar.

### 1.2 Rumusan Masalah

Adapun masalah yang diangkat pada penelitian ini adalah apakah pemberian sukrosa 1%, 2%, 4% berpengaruh terhadap jumlah nekrosis inti hepatosit dan steatosis hepatosit pada Ikan Zebra *(Danio rerio)*?

### 1.3 Tujuan Penelitian

Adapun tujuan penelitian ini adalah untuk mengetahui pengaruh pemberian sukrosa 1%, 2%, 4% terhadap jumlah nekrosis inti hepatosit dan steatosis hepatosit pada Ikan Zebra *(Danio rerio)*.

### 1.4 Manfaat Penelitian

Penelitian ini diharapkan dapat memberikan manfaat teoritis dan praktis sebagai berikut :

#### 1.4.1 Manfaat Teoritis

Sebagai landasan teori berbasis penelitian eksperimental *in vivo* untuk mengetahui efek perbedaan kadar sukrosa terhadap perubahan histologi jaringan organ hepar Ikan Zebra (*Danio rerio*).

#### 1.4.2 Manfaat Praktis

Pengembangan penelitian model hiperglikemia pada Ikan Zebra *(Danio rerio).*

# BAB VII
# KESIMPULAN DAN SARAN

## 7.1 Kesimpulan

Berdasarkan hasil penelitian dapat disimpulkan bahwa:

1. Pemberian sukrosa dengan konsentrasi 1%, 2%, dan 4% selama 28 hari pada ikan zebra menyebabkan peningkatan jumlah sel hepar yang mengalami nekrosis inti hepatosit dan steatosis.
2. Semakin tinggi konsentrasi sukrosa, semakin banyak sel hepar yang mengalami nekrosis inti hepatosit dan steatosis.

## 7.2 Saran

1 Saran untuk memperbaiki keterbatasan penelitian ini

a. Menggunakan ikan zebra betina untuk mengetahui pengaruh hormonal terutama estrogen terhadap kerusakan hepar yang terjadi akibat pemberian sukrosa.

b. Menggunakan model hewan coba yang lebih besar untuk mengetahui indikator-indikator kerusakan hepar lainnya akibat pemberian sukrosa, seperti kadar enzim transaminase (SGOT dan SGPT), serta penanda stress oksidatif seperti superoxide dismutase (SOD) dan malanondialdehyde (MDA).

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