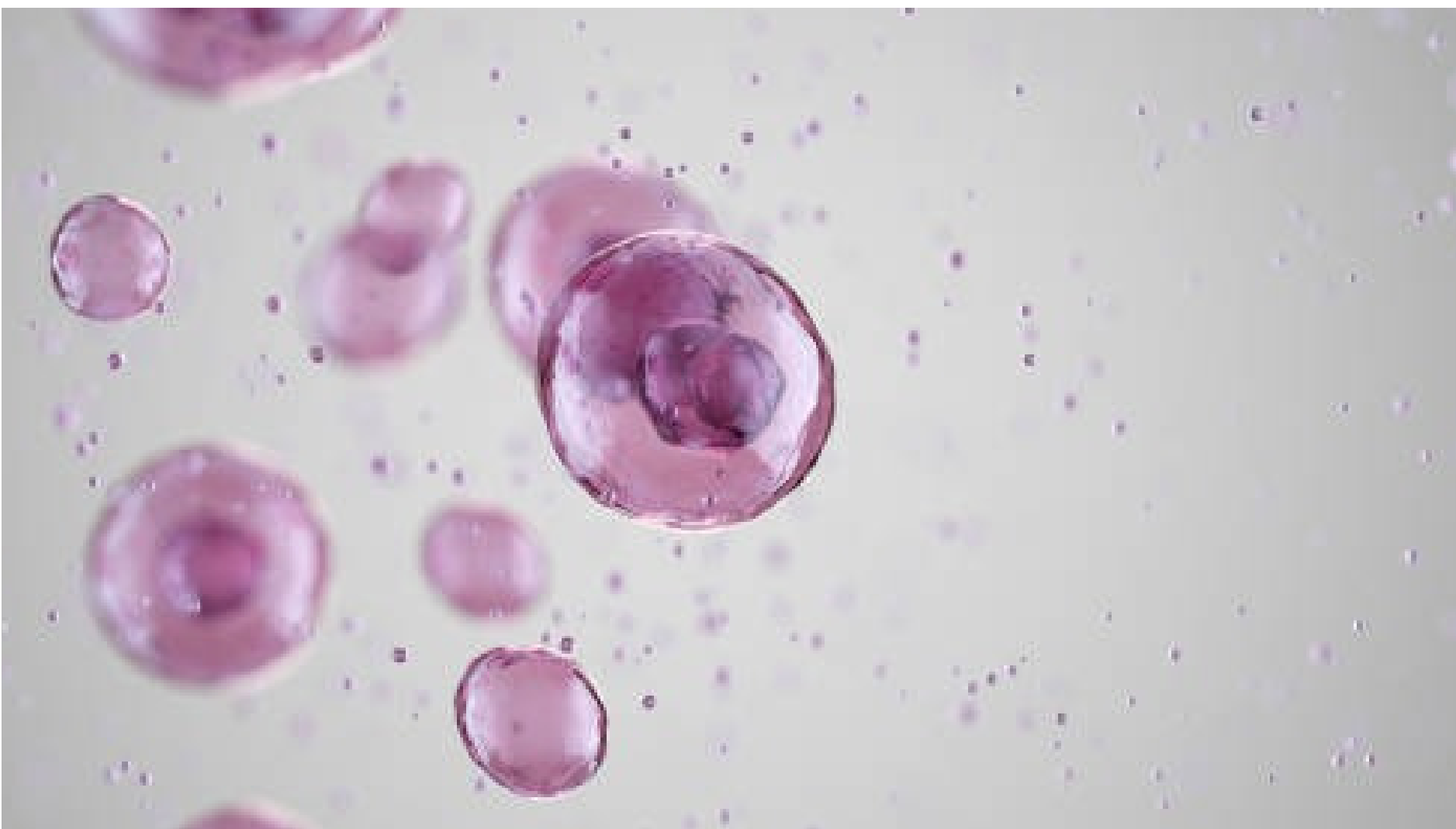


LATAR BELAKANG

Gasotransmitter seperti nitrit oksida (NO), karbon monoksida (CO), dan hidrogen sulfida (H₂S) merupakan molekul gas kecil yang diproduksi endogen dalam tubuh dan berperan penting dalam regulasi vaskular dan perlindungan terhadap stres oksidatif. Meskipun awalnya dikenal sebagai zat beracun, pada dosis rendah gasotransmitter memiliki manfaat terapeutik melalui mekanisme hormesis, di mana dosis kecil memberikan efek perlindungan, sementara dosis tinggi bersifat toksik. Tantangan utama dalam penggunaannya adalah kestabilan gas yang rendah dan risiko toksisitas pada dosis tinggi. Inovasi teknologi gelembung nano menjadi solusi efektif untuk penghantaran gasotransmitter karena mampu menembus jaringan target seperti tumor, menghindari sistem imun, dan meningkatkan akumulasi di lokasi terapi. Dengan ukuran kurang dari 1 μm dan stabilitas tinggi dalam cairan biologis, gelembung nano dapat meningkatkan efektivitas terapi oksigenasi jaringan hipoksia, kanker, dan penyakit kardiovaskular sambil meminimalkan risiko toksisitas.

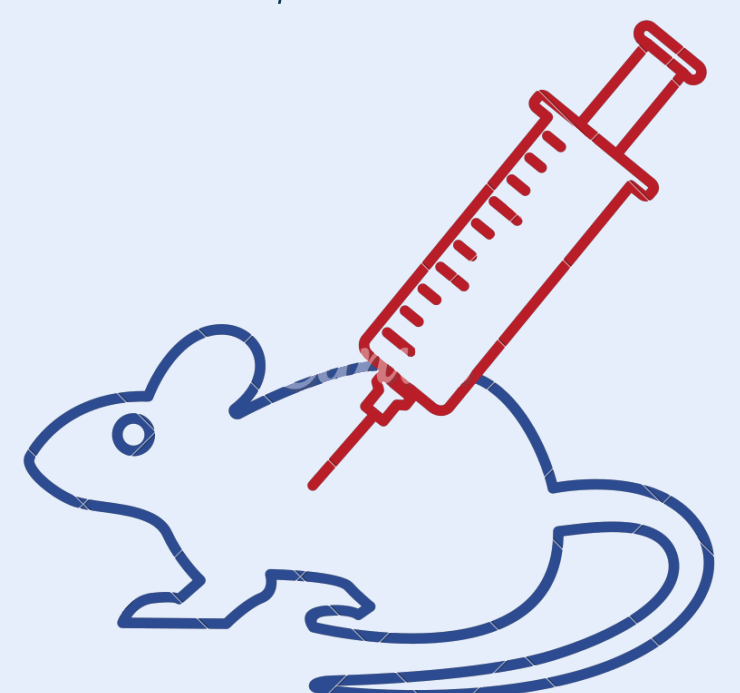
Selain gasotransmitter, gas oksihidrogen (HHO) juga menunjukkan potensi sebagai agen terapeutik berkat sifat antioksidan, anti-inflamasi, dan antitumornya. HHO terbukti mampu menghambat proliferasi sel kanker, memicu apoptosis, dan mengurangi stres oksidatif. Penelitian ini dirancang untuk mengevaluasi pengaruh gelembung nano HHO terhadap perkembangan kanker hati menggunakan model tikus Wistar (*Rattus norvegicus*), serta mengkaji toksisitas kombinasi gelembung nano gasotransmitter melalui pengukuran IC₅₀ (in vitro) dan LD₅₀ (in vivo). Evaluasi ini penting untuk menentukan rasio optimal gasotransmitter dan memastikan keamanan serta efektivitasnya sebelum penerapan klinis. Melalui analisis molekuler dan histopatologi, penelitian pengaruh gelembung nano HHO diharapkan dapat membuka peluang pengembangan terapi kanker hati berbasis teknologi nano yang lebih efektif dan minim efek samping.



- Durasi penelitian : 2024-2026
- Pendanaan : Reverse Aging and Homeostasis (RAHO) Club

TUJUAN PENELITIAN

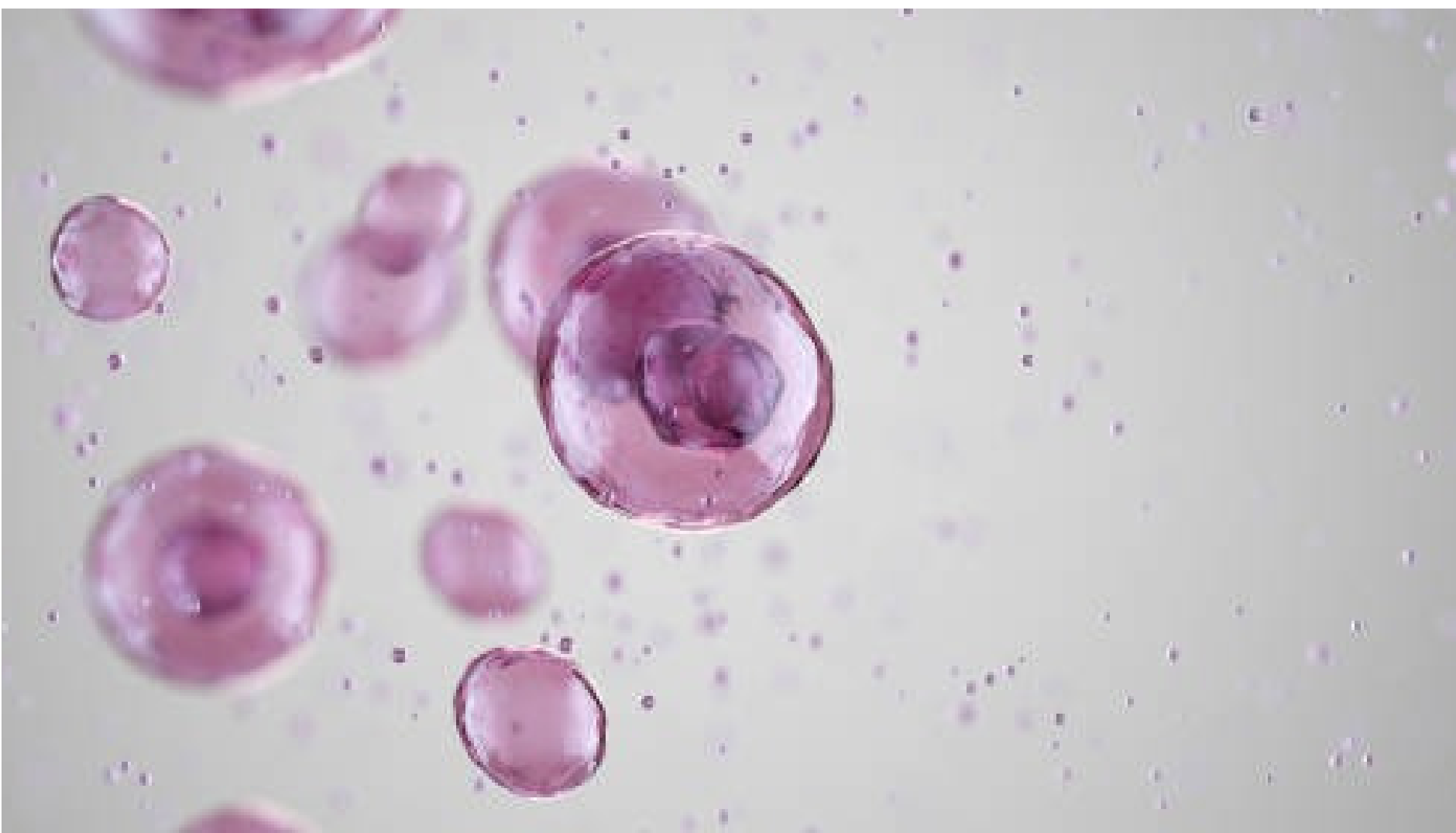
1. Mengevaluasi toksisitas kombinasi gelembung nano gasotransmitter (NO, CO, H₂S) melalui pengukuran viabilitas sel (IC₅₀) dan tingkat toksisitas akut (LD₅₀) pada model hewan, serta menganalisis, patologis, dampak dan gejala toksisitas
2. Membandingkan efektivitas kombinasi gelembung nano gasotransmitter dalam memengaruhi viabilitas sel dan mengidentifikasi potensi penggunaannya sebagai agen terapeutik berbasis nanoteknologi yang aman dan efisien.
3. Mengetahui pengaruh campuran gelembung nano oksihidrogen (HHO) terhadap perkembangan kanker hati (proliferasi, apoptosis, dan pemanjangan telomere) pada tikus model.
4. Mengetahui perbandingan efektivitas gelembung nano HHO dengan obat kanker hati yang digunakan dalam kontrol positif.



INTRODUCTION

Gasotransmitters such as nitric oxide (NO), carbon monoxide (CO), and hydrogen sulfide (H₂S) are small gas molecules produced endogenously in the body, playing a crucial role in vascular regulation and protection against oxidative stress. Although initially recognized as toxic substances, at low doses, gasotransmitters offer therapeutic benefits through the hormesis mechanism, where small doses provide protective effects, while high doses become toxic. The main challenges in their application include low gas stability and toxicity risks at high concentrations. The innovation of nanobubble technology serves as an effective solution for gasotransmitter delivery, as it can penetrate target tissues such as tumors, evade the immune system, and enhance accumulation at therapy sites. With a size of less than 1 μm and high stability in biological fluids, nanobubbles can improve the effectiveness of hypoxic tissue oxygenation therapy, cancer treatment, and cardiovascular disease therapy while minimizing toxicity risks.

In addition to gasotransmitters, oxyhydrogen gas (HHO) has also demonstrated potential as a therapeutic agent due to its antioxidant, anti-inflammatory, and antitumor properties. HHO has been shown to inhibit cancer cell proliferation, induce apoptosis, and reduce oxidative stress. This study is designed to evaluate the impact of HHO nanobubbles on liver cancer progression using Wistar rat (*Rattus norvegicus*) models, as well as to assess the toxicity of gasotransmitter nanobubbles through IC₅₀ (in vitro) and LD₅₀ (in vivo) measurements. This evaluation is crucial in determining the optimal gasotransmitter ratio and ensuring its safety and efficacy before clinical application. Through molecular and histopathological analyses, research on the effects of HHO nanobubbles is expected to open new opportunities for the development of nanotechnology-based liver cancer therapies that are more effective and have minimal side effects.



- Research Duration : 2024-2026
- Funding : Reverse Aging and Homeostasis (RAHO) Club

GOALS

1. Evaluate the toxicity of the gasotransmitter nanobubble combination (NO, CO, H₂S) through IC₅₀ (cell viability) and LD₅₀ (acute toxicity in animal models) measurements, as well as analyze pathological effects, impacts, and toxicity symptoms.
2. Compare the effectiveness of the gasotransmitter nanobubble combination in influencing cell viability and identify its potential as a safe and efficient nanotechnology-based therapeutic agent.
3. Assess the impact of oxyhydrogen (HHO) nanobubbles on liver cancer progression, focusing on cell proliferation, apoptosis, and telomere length in animal models.
4. Determine the comparative effectiveness of HHO nanobubbles against conventional liver cancer drugs used as a positive control.

