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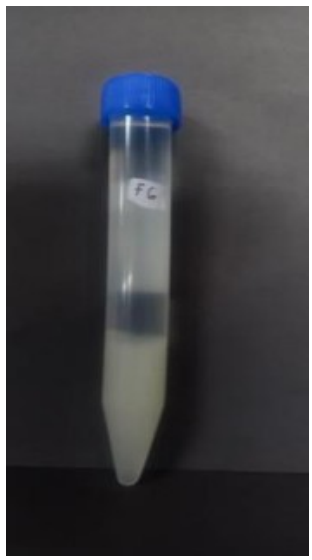
LAMPIRAN

Lampiran 1.

Formulasi Nanoemulsi





Lampiran 2.

Uji Tipe Emulsi

Lampiran 3.

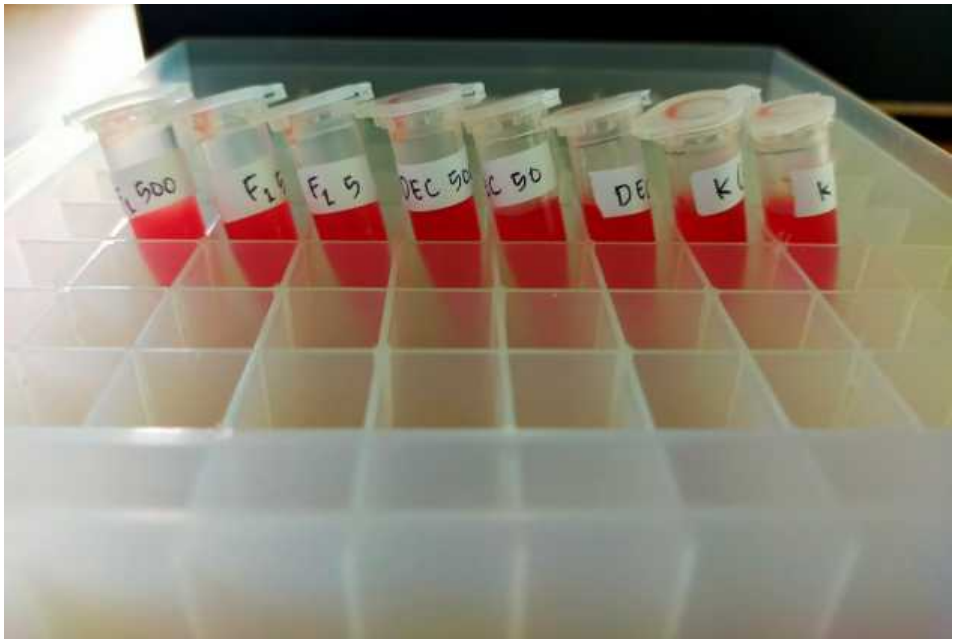
Uji In Vitro

Lampiran 4.

Uji Ex Vivo Permeasi dan Retensi

Lampiran 5.

Uji Hemolisis



Lampiran 6.

Uji Iritasi dan Histopatologi

Lampiran 7.

Persetujuan Etik oleh Komisi Etik Penelitian Kesehatan FK-UH.

KEMENTERIAN PENDIDIKAN, KEBUDAYAAN, RISET DAN TEKNOLOGI
UNIVERSITAS HASANUDDIN FAKULTAS KEDOKTERAN
KOMITE ETIK PENELITIAN KESEHATAN
RSPTN UNIVERSITAS HASANUDDIN
RSUP Dr. WAHIDIN SUDIROHUSODO MAKASSAR
Sekretariat : Lantai 2 Gedung Laboratorium Terpadu
JL.PERINTIS KEMERDEKAAN KAMPUS TAMALANREA KM.10 MAKASSAR 90245.
Contact Person dr. Agussalim Bukhari, M.Med.PhD, SpGK TELP. [illegible]

REKOMENDASI PERSETUJUAN ETIK
Nomor : 488/UN4.6.4.5.31/ PP36/ 2021

Tanggal: 28 Juli 2021

Dengan ini Menyatakan bahwa Protokol dan Dokumen yang Berhubungan Dengan Protokol berikut ini telah mendapatkan Persetujuan Etik :

No Protokol	UH21060398	No Sponsor Protokol	
Peneliti Utama	**Hanin Azka Qanita**	Sponsor	
Judul Peneliti	Lymphatic Targeting dari Sediaan Emulsi Dietilkarbamazin Tipe Air dalam Minyak sebagai Peningkat Efektivitas Terapi Penyakit Kaki Gajah (Elephantiasis)		
No Versi Protokol	1	Tanggal Versi	**25 Juni 2021**
No Versi PSP		Tanggal Versi	
Tempat Penelitian	**Fakultas Farmasi Universitas Hasanuddin Makassar**		
Jenis Review	☐ Exempted ☒ Expedited ☐ Fullboard Tanggal	Masa Berlaku 28 Juli 2021 sampai 28 Juli 2022	Frekuensi review lanjutan
Ketua Komisi Etik Penelitian Kesehatan FKUH	Nama **Prof.Dr.dr. Suryani As'ad, M.Sc.,Sp.GK (K)**	Tanda tangan	
Sekretaris Komisi Etik Penelitian Kesehatan FKUH	Nama dr. Agussalim Bukhari, M.Med.,Ph.D.,Sp.GK (K)	Tanda tangan	

Kewajiban Peneliti Utama:

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum di implementasikan
- Menyerahkan Laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan lapor SUSAR dalam 72 Jam setelah Peneliti Utama menerima laporan
- Menyerahkan Laporan Kemajuan (progress report) setiap 6 bulan untuk penelitian resiko tinggi dan setiap setahun untuk penelitian resiko rendah
- Menyerahkan laporan akhir setelah Penelitian berakhir
- ...pangan dari prokol yang disetujui (protocol deviation / violation)
- ...ruran yang ditentukan

Lampiran 8.

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Development water in oil nanoemulsion of diethylcarbamazine for enhanced the characteristics for lymphatic targeting: A proof of concept study

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ABSTRACT

As an antifilariasis drug, oral administration of diethylcarbamazine (DEC) could not effectively deliver the drug to the lymphatic system. Hydrophobic formulation with a particle size of <100 nm could improve the delivery of drug. Accordingly, we developed water in oil nanoemulsion encapsulating DEC. The nanoemulsion was less than 100 nm with negative charge, showing its suitability for lymphatic targeting. The nanoemulsion could sustain the release of DEC and improve the retention in intestinal tissue in comparison with DEC solution. Importantly, this approach did not cause any hemolysis in *in vitro* study and any irritation in *in vivo* study.

1. Introduction

According to data from the WHO in 2010, more than 120 million people in 83 countries were infected with lymphatic filariasis (LF), of whom about 40 million have been disabled or paralyzed by it. Its distribution extends from Latin America, across central Africa, southern Asia, and into the Pacific islands [1]. Furthermore, WHO has reported that around 51 countries still require LF treatment using mass drug administration (MDA). As one of drugs used in MDA, diethylcarbamazine (DEC) been used through oral administration with a dose of 6mg/KgBB/day for 12 days [2].

In LF disease, the adult filarial stay in the lymphatic system. Therefore, it is important to ensure that the drug is delivered in the lymphatic system for effective therapy. In order to reach the lymphatic system, drugs administered orally must have a good lipophilicity and log P value of >4.7 [3]. Nevertheless, DEC is hydrophilic drug with log P value of 0.3. With this in mind, it is unlikely that oral administration could not deliver DEC to the infection site. Our previous study showed the limited concentration of DEC after conventional oral administration. Therefore, an effective drug delivery system is needed in order to reach the target of the lymphatic system for effectiveness of the treatment of LF.

Several delivery systems have been developed to improve the delivery of drugs to the lymphatic system. However, most of the methods require complicated technique with sophisticated instrument. Nanoemulsion, especially water in oil type, was considered as the appropriate system due to the high lipophilicity of oil used in the oil phase, which can be prepared by simple method. Nanoemulsion is one of the types of emulsion that have a drip that can reach less than 500 nm [4]. The nanoemulsion water-in-oil (W/O) is a type of emulsion with nanometric droplets that surfactant made the droplets dispersed in the oil phase [5,6]. Nanoemulsion can increase the permeability and retention effects on the target tissue [7]. Nanoemulsion has been reported to be absorbed directly into the lymphatic system and can avoid the metabolism of the first line of the liver so that the drug's bioavailability increases [8]. Considering all these backgrounds, here, for the first time, we developed W/O nanoemulsion containing DEC for improved treatment of LF. The nanoemulsion was characterized for their physical properties. Specifically, the *ex vivo* intestinal permeation study was investigated. Finally, *in vitro* toxicity and *in vivo* intestinal irritation were evaluated.

2. Material and methods

2.1. Formulation and screening of water in oil nanoemulsion

The nanoemulsions were prepared using simple homogenization method. Tween®80 and Span®80 were used as stabilizers for water and

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