

ABSTRACT

The purpose of this research is to create a micro-emulgel and suppositories to cure hemorrhoids with natural ingredients like chicken bile and the *Teucrium polium* extracts. Because ethanol maceration is a straightforward and economical method, we first used it to extract the bioactive components. While several ratios were attempted to identify the ideal extraction conditions for chicken bile, *Teucrium polium* extraction was optimized using a Box-Behnken design. The main response variables chosen were the total phenolic compounds and the extraction yield. The biological activities of *Teucrium polium* and chicken bile extracts were assessed after optimization, with an emphasis on their anti-inflammatory, antibacterial, and antioxidant abilities. These results led us to devise a formulation technique. In order to improve the suppository formulation, several excipient ratios were tried, and the best combination was eventually found. An ideal formulation of the micro-emulgel was achieved by optimizing spreadability and viscosity by the use of a mixture. lattice design.

Key words:

Hemorrhoids, chicken bile *Teucrium Polium*, maceration, optimization, box behnken design, mixture lattice design, biological activities, suppositories, microemulgel.

RESUME

Le but de ce travail est de formuler un micro-émulgel et des suppositoires pour guérir les hémorroïdes avec des ingrédients naturels tels que la bile de poulet et la plante *Teucrium polium*. L'extraction par macération à l'éthanol étant une méthode simple et économique, nous l'avons d'abord utilisée pour extraire les composants bioactifs. Alors que plusieurs ratios ont été tentés pour identifier les conditions d'extraction idéales pour la bile de poulet, l'extraction de *Teucrium polium* a été optimisée à l'aide d'un plan de Box-Behnken. Les principales variables de réponse choisies étaient la teneur totale en composés phénoliques et le rendement d'extraction. Les activités biologiques des extraits de *Teucrium polium* et de bile de poulet ont été évaluées après optimisation, particulièrement les activités anti-inflammatoires, antibactériennes et antioxydantes. Ces résultats nous ont amenés à concevoir une technique de formulation. Afin d'améliorer la formulation des suppositoires, plusieurs ratios d'excipients ont été essayés, et la meilleure combinaison a finalement été trouvée. Une formulation idéale du micro-émulgel a été obtenue en optimisant l'étalement et la viscosité par l'utilisation d'un plan de mélange.

Mots clés :

Hémorroïdes, bile de poulet *Teucrium Polium*, macération, optimisation, plan box behnken, plan de mélange, activités biologiques, suppositoires, microémulgel.

TABLE OF CONTENT

List of Abbreviations	vii
List of Figures	ix
List of Tables	x
Abstract	xi
GENERAL INTRODUCTION	1
CHAPTER I: LITERATURE REVIEW	
I.1. <i>Teucrium Polium</i>	3
I.1.1. Botanical description of <i>Teucrium Polium</i>	3
I.1.2. Vernacular names.....	4
I.1.3. Taxonomy and systematics	4
I.1.4. Traditional and medical usage properties	4
I.2. Animal waste valorisation	5
I.2.1. Gallbladder (bile).....	5
I.2.2. Animal fat	5
I.3. Secondary metabolites of plants	5
I.3.1. Flavonoids.....	6
I.3.2. Coumarins	6
I.3.3. Tannins.....	6
I.4. Biological activities of phenolic compounds.....	6
I.4.1. Antioxidant activity	6
a. DPPH activity	7
b. ABTS activity	7
c. FRAP activity	8
d. Silver nanoparticles (SNP)	8
e. Phenanthroline	8

I.4.2. Anti-bacterial activity	8
I.4.3. Anti-inflammatory activity	9

CHAPTER II: MATERIALS AND METHODS

II.1. Materials.....	10
II.1.1. Products	10
II.1.2. Laboratory instruments.....	12
II.1.3. Softwares	13
II.2. Methods.....	13
II.2.1. Extraction of <i>Teucrium polium</i>	13
II.2.2. Extraction of Chicken Bile	15
II.2.3. Characterization of extracts	15
II.2.4. Determination of the chemical properties of Goat Fat	24
II.2.5. Formulation of suppositories	26
II.2.6. Optimization of an emulgel by mixture design	28
II.2.7. <i>In vitro</i> irritation test (HET-CAM test)	30

CHAPTER III: RESULTS AND DISCUSSION

III.1. Optimization of <i>Teucrium polium</i> extraction.....	32
III.1.1. Statistical analysis	32
III.1.2. Graphical analysis	34
III.1.3. Determination of the optimum	36
III.2. Chicken bile extraction	38
III.3. Analysis of extracts by Fourier infrared transform spectrometer (FTIR).....	39
III.4. Biological activities	41
III.4.1. Anti-oxidant activities	41
III.4.2. Anti-bacterial activity.....	45
III.4.3. Anti-inflammatory activity.....	48
III.4.4. Sun protection factor (SPF).....	49

III.5. Suppositories formulation	50
III.5.1. Characterization of Goat fat	50
III.5.2. Formulation of Suppositories	51
III.6. Emulgel formulation	54
III.6.1. Ternary phase diagram	54
III.6.2. Optimization of microemulgel	55
III.7. <i>In vitro</i> irritation test (HET-CAM test).....	62
GENERAL CONCLUSION	64
REFERENCES	66
APPENDIX	

DEMOCRATIC AND POPULAR REPUBLIC OF ALGERIA
MINISTRY OF HIGHER EDUCATION AND RESEARCH SCIENTIFIC
UNIVERSITY OF SALAH BOUBNIDER, CONSTANTINE 3



FACULTY OF PROCESS ENGINEERING
DEPARTMENT OF PHARMACEUTICAL ENGINEERING

N° d'ordre :... ..
Série :... ..

Master's Thesis

Course: Process Engineering

Option: Pharmaceutical Process Engineering

OPTIMIZATION AND FORMULATION OF PHARMACEUTICAL PRODUCTS FOR HEMORRHOIDS THERAPY

Directed by:

BADAoui Fatima Zohra

Associate Professor-A-

Presented by:

BAKHOUCHE Abdellah

BECHKRI Soheib

DJELMAMI HANI Soufiane

Academic year: 2023-2024

session: June