

Summary Report

Thymol iodide

Prepared for:

Food and Drug Administration
Clinical use of bulk drug substances nominated for inclusion on the 503B Bulks
List
Grant number: 5U01FD005946

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December 2020

This report was supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award (U01FD005946) totaling \$2,342,364, with 100 percent funded by the FDA/HHS. The contents are those of the authors and do not necessarily represent the official views of, nor an endorsement by, the FDA/HHS or the U.S. Government.

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Frequently Used Abbreviations

API	Active Pharmaceutical Ingredient
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
IRB	Institutional Review Board
OTC	Over-the-counter
ROA	Route of administration
SME	Subject matter expert
UK	United Kingdom
US	United States

INTRODUCTION

This report was created to assist the Food and Drug Administration (FDA) in their evaluation of the use of thymol iodide (UNII code: A51HJM3XSU), which was nominated for use as a bulk drug substance in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act.

The aim of this report was to describe how thymol iodide is used in clinical research and practice to diagnose, prevent, or treat disease. Due to the broad, exploratory nature of this aim, scoping review methodology was used. Following the scoping review framework, a systematic literature review was conducted and healthcare practitioners were consulted to identify how thymol iodide has been used historically and currently.¹⁻³ Assessment of study quality and risk of bias were not performed because the aim of this report was not to make specific recommendations on the use of this substance in clinical practice.^{1,4,5} Rather, the aim was to summarize the available evidence on the use of thymol iodide and thereby assist the FDA to determine whether there is a need for the inclusion of this substance on the 503B Bulks List.

REVIEW OF NOMINATION

Thymol iodide was nominated for inclusion on the 503B Bulks List by the American Society of Health-System Pharmacists (ASHP). Thymol iodide was nominated as an absorbent and protective agent with antimicrobial properties via the topical route of administration.

The nominator did not provide references from published peer-reviewed literature to describe the pharmacology and support the clinical use of thymol iodide.

The nominator did not provide reasons for nomination to the 503B Bulks List.

METHODOLOGY

Background information

The national medicine registers of 13 countries and regions were searched to establish the availability of thymol iodide products in the United States (US) and around the world. The World Health Organization, the European Medicines Agency (EMA), and globalEDGE were used to identify regulatory agencies in non-US countries. The medicine registers of non-US regulatory agencies were selected for inclusion if they met the following criteria: freely accessible; able to search and retrieve results in English language; and desired information, specifically, product trade name, active ingredient, strength, form, route of administration (ROA), and approval status, provided in a useable format. Based on these criteria, the medicine registers of 13 countries/regions were searched: US, Canada, European Union (EU), United Kingdom (UK), Ireland, Belgium, Latvia, Australia, New Zealand, Saudi Arabia, Abu Dhabi, Hong Kong, and Namibia. Both the EMA and the national registers of select EU countries (Ireland, UK, Belgium, and Latvia) were searched because some medicines were authorized for use in the EU and not available in a member country and vice versa.

Each medicine register was searched for thymol iodide; name variations of thymol iodide were entered if the initial search retrieved no results. The following information from the search results of each register was recorded in a spreadsheet: product trade name; active ingredient; strength; form; ROA; status and/or schedule; approval date. Information was recorded only for products with strengths, forms, and/or ROA similar to those requested in the nominations.

In addition to the aforementioned medicine registers, the DrugBank database (version 5.1.5) and the Natural Medicines database were searched for availability of over-the-counter (OTC) products containing

thymol iodide. The availability of OTC products (yes/no) in the US and the ROA of these products were recorded in a spreadsheet. Individual product information was not recorded.

Systematic literature review

Search strategy

A medical librarian constructed comprehensive search strategies for Ovid MEDLINE and Embase. The search strategies used a combination of controlled vocabulary terms and keywords to describe three concepts: thymol iodide, topical administration or form, and therapeutic use (refer to Appendix 1 for full search strategies). Keywords for brand or proprietary products were not included in the search strategy because studies that utilized such products were excluded. Results were limited to human studies in English language. Searches were conducted on December 22, 2019. The reference lists of relevant systematic reviews and meta-analyses, retrieved in a separate search of Ovid MEDLINE on November 9, 2019, were reviewed to identify additional studies. In addition, the ECRI Guidelines Trust[®] repository was searched on November 9, 2019 for clinical practice guidelines that recommended the use of thymol iodide and provided sufficient information on dosing and administration.

Results were exported to EndNote for Windows version X9.2 (Clarivate Analytics), and duplicates were removed. The de-duplicated results were uploaded to Covidence (Veritas Health Innovation) for screening.

Study selection

Studies in which thymol iodide was used in the nominated dosage form, ROA, and/or combination product to diagnose, prevent or treat the nominated disease or condition, or other conditions not specified in the nomination, were included. Studies were excluded if they were: written in a language other than English; reviews or meta-analyses; surveys or questionnaires (cross-sectional design); designed to evaluate cost-effectiveness, mechanism of action, pre-clinical use, safety, or toxicity; or any study design other than a randomized controlled trial conducted in a non-US country. Studies were also excluded if thymol iodide was used as: a brand or proprietary product; an FDA-approved product in the nominated dosage form, ROA, or combination; or a dosage form, ROA, or combination that was not nominated. Studies in which thymol iodide was used to diagnose, prevent, or treat autism were excluded due to a separate project examining the use of compounded substances in individuals with autism. Studies that did not meet the inclusion criteria but provided valuable information about the pharmacological or current or historical use of the substance were noted and put in a separate group in the EndNote library. Two reviewers independently screened titles and abstracts and reviewed full-text articles. A third reviewer reconciled all disagreements.

Data extraction

The following information was recorded in a standard data extraction form: author names; article title; journal; year of publication; country; study type; historical use of thymol iodide; setting; total number of patients; number of patients who received thymol iodide; patient population; indication for use of thymol iodide; dosage form and strength; dose; ROA; frequency and duration of therapy; use of thymol iodide in a combination product; use and formulation of thymol iodide in a compounded product; use of thymol iodide compared to FDA-approved drugs or other treatments; outcome measures; authors' conclusions. One reviewer extracted data from the included studies; a second reviewer checked the data extraction.

Interviews

Semi-structured interviews with subject matter experts (SMEs) were conducted to understand how and in what circumstances thymol iodide was used in a clinical setting. The systematic literature review and the indications from the nomination were reviewed to identify the following medical specialties that would potentially use thymol iodide: dentistry and oral medicine, dermatology, primary care and internal medicine, and surgery. Potential SMEs within the relevant medical specialties were identified through recommendations and referrals from professional associations, colleagues' professional networks, and authors of relevant literature. In addition, the American Society of Health-System Pharmacists (ASHP) and select outsourcing facilities were contacted for interviews and referrals to additional SMEs. SMEs provided oral informed consent to be interviewed and audio recorded. Interviews lasting up to 60 minutes were conducted via telephone, audio recorded, and professionally transcribed. The transcriptions and notes were entered into NVivo 12 (QSR International) for qualitative data analysis. Several members of the research team independently coded the transcriptions of two representative interviews for themes. The team members discussed the codes that emerged from their independent analysis, as well as those codes that were determined a priori. The code book was developed out of the integration of these coding schemes.

Survey

A survey was distributed to the members of professional medical associations to determine the use of thymol iodide in clinical practice. The online survey was created using Qualtrics® software (refer to Appendix 2 for complete survey). A Google™ search was conducted to identify the professional associations in the US for the relevant medical specialties. An association's website was searched to identify the email of the executive director, regulatory director, media director, association president, board members, or other key leaders within the organization to discuss survey participation. If no contact information was available, the "contact us" tab on the association website was used. An email describing the project and requesting distribution of the survey to the association's members was sent to the identified person(s). Associations that declined, did not respond, or did not provide significant data in project Year 1 were not contacted to distribute the project Year 2 surveys.

The survey was posted on the project website and the survey link was distributed to the associations that agreed to participate (refer to Appendix 3 for associations that participated and those that did not).

Participation was anonymous and voluntary. The estimated time for completion was 15 minutes with a target of 50 responses per survey.

The University of Maryland, Baltimore Institutional Review Board (IRB) and the FDA IRB reviewed the interview and survey methods and found both to be exempt. The Office of Management and Budget approved this project.

CURRENT AND HISTORIC USE

Results of background information

- Thymol iodide is not available as an FDA-approved product in the nominated dosage form and ROA.
- Thymol iodide is available in various topical dosage forms as an OTC product in the US.
- There is no current United States Pharmacopeia (USP) monograph for thymol iodide. There is a USP monograph for thymol.
- Thymol iodide is not available in the nominated dosage form and ROA in any of the foreign medicine registries searched.

Table 1. Currently approved products – US

No approved products in the US

Table 2. Currently approved products – select non-US countries and regions

No approved products in the selected non-US countries and regions

Results of literature review

Study selection

Database searches yielded 582 references; 1 additional reference was identified from searching ECRI Guidelines Trust® and the references of relevant systematic reviews. After duplicates were removed, 413 titles and abstracts were screened. After screening, the full text of 101 articles were reviewed. Finally, 0 studies were included. One hundred one studies were excluded for the following reasons: thymol iodide used as brand or proprietary product (41 studies); wrong study design (28); wrong dosage form or ROA (16); thymol iodide not used clinically (7); wrong substance (3); thymol iodide only mentioned briefly (3); language other than English (2); duplicate study (1).

Refer to Figure 1 for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Characteristics of included studies

No studies were included from the literature review

Use of thymol iodide

No studies were included from the literature review

Pharmacology and historical use

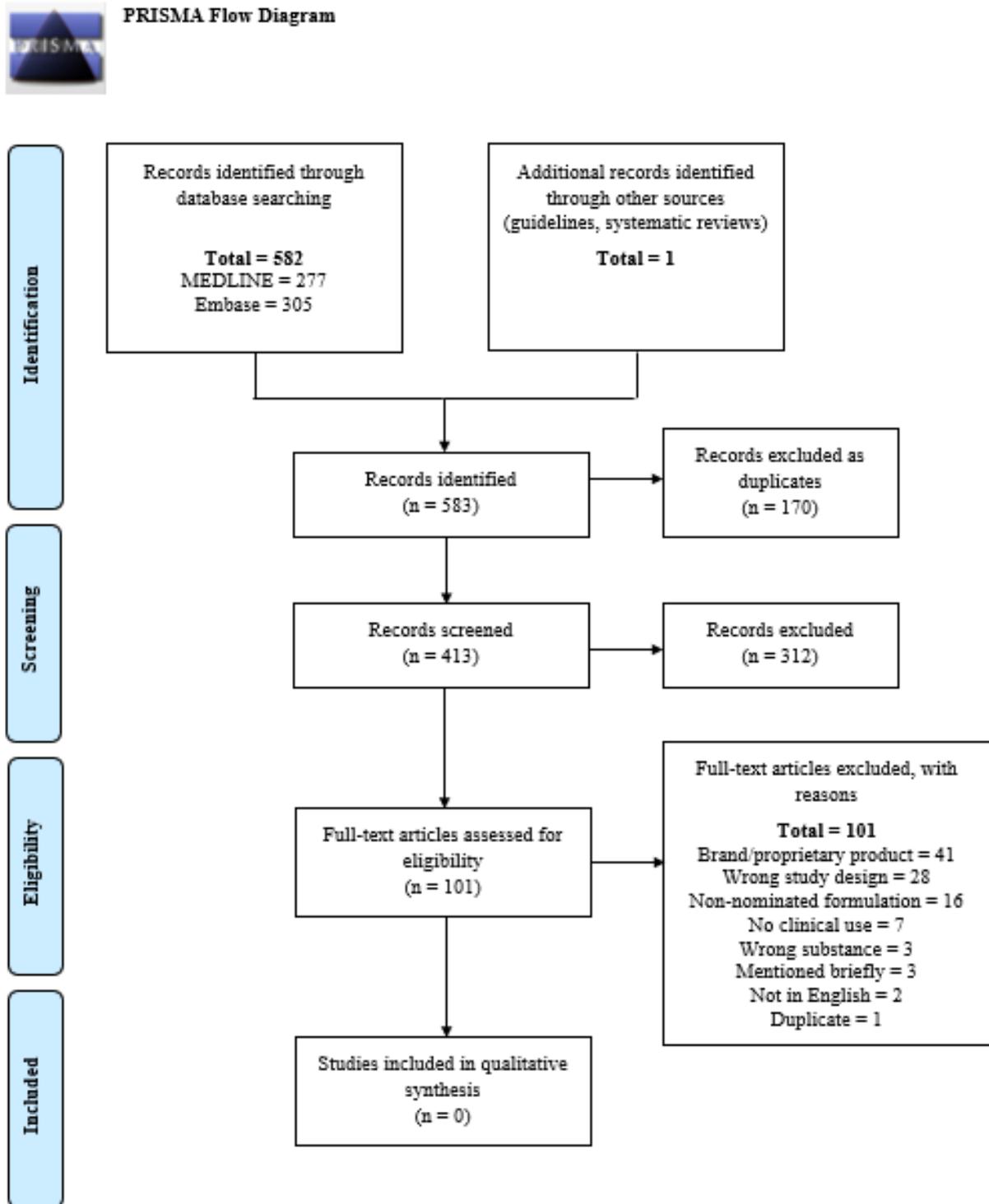
There were 8 studies identified that did not meet the inclusion criteria but provided valuable information about the pharmacology and historical use of thymol iodide.

Thymol can inhibit dental plaque growth and is an ingredient in some mouth rinses and chlorhexidine-containing dental varnishes.⁶ Cervitec®, a varnish containing chlorhexidine and thymol, has antimicrobial effects in vitro against many Gram positive and negative bacteria and

yeast.^{7,8} Chlorhexidine is known to have activity against oral microflora and this varnish is used to prevent and stop root demineralization as well as proposed to treat hypersensitivity after mechanical periodontal therapy.⁷ Maisto's paste, which is made of zinc oxide, thymol, chlorphenol camphor, and lanolin, was another topical formulation mentioned for endodontic treatment of infected primary teeth.^{9,10}

Other indications for the use of thymol formulations included a topical 4% thymol to help keep the nail folds and surrounding skin dry during treatment of chronic paronychia,¹¹ a topical lavender-thymol oil for promoting episiotomy healing,¹² and a suspension with talc and thymol iodine for pleurodesis.¹³

Figure 1. PRISMA flow diagram showing literature screening and selection.



Adapted from:
Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol.* 2009;62(10):1006-1012. Available from: <http://www.prisma-statement.org/>.

Table 3. Types of studies

No studies included

Table 4. Number of studies by country

No studies included

Table 5. Summary of included studies

No studies included

Table 6. Dosage by indication – US

No studies included

Table 7. Dosage by indication – non-US countries

No studies included

Table 8. Number of studies by combination

No combination products were nominated

Table 9. Compounded products – US

No studies included

Table 10. Compounded products – non-US countries

No studies included

Results of interviews

Two hundred eighty-five SMEs were contacted for interviews; 96 agreed to be interviewed, and 189 declined or failed to respond to the interview request. Six SMEs discussed thymol iodide. Amongst these 6 SMEs, there were 5 dentists and 1 medical doctor. The SMEs specialized and/or were board-certified in dentistry and dermatology, working in academic medical centers, consultancy, private practice, and 2 were retired. The SMEs had been in practice for 5 to 40 years.

Most SMEs were not familiar with and did not use thymol iodide. Thymus oil has broad-spectrum antimicrobial properties and when iodinated, there could be some absorbent capacity that could potentially be useful for wound healing in patients with leg ulcers, decubiti, or bad intertrigo. One SME stated that thymol could be used as a mouth wash, like using Listerine® at home. As a prescription, chlorhexidine would be given as the antimicrobial. Thymol is similar to diluted Betadine® (povidone-

iodine), since it has a concentration of 0.12% instead of 4%, used in surgery to disinfect the site. The SME stated that it would be great if there was an alternative to decrease mouth pathogens.

Results of survey

Four people responded to the survey distributed via professional medical associations and available on the project website; refer to Table 11 for respondent characteristics.

Among respondents, 3 (75%), used thymol iodide, with 1 (33%) using thymol iodide for pseudomonas of the nails and 1 (33%) for onychomycosis and mold in nails (refer to Table 12).

Amongst the 3 respondents who used thymol iodide, 2 (67%) used thymol iodide as a compounded drug product. One of the survey respondents who used thymol iodide did not provide a response. Survey respondents utilized compounded thymol iodide due to lack of commercial products in an appropriate dosage form, strength or combination (25% of respondents), patient allergies (0%), other patient conditions preventing use of commercial products (25%), or no commercially available products with thymol iodide (50%). Refer to Table 13 for reasons for using compounded thymol iodide.

The two respondents who used compounded thymol iodide (100%) did not stock non-patient-specific compounded thymol iodide at their practice (refer to Table 14). No respondents provided a response for how they obtained compounded thymol iodide.

Table 11. Characteristics of survey respondents

Terminal Clinical Degree	Responses, n (N=4)
Doctor of Medicine (MD)	2
Doctor of Pharmacy (PharmD) or Bachelor of Science in Pharmacy (BS Pharm)	1
No Response	1
Practice Setting	Responses, n (N=4)
Physician office or private practice	2
Academic medical center	1
No response	1

Table 12. Conditions for which thymol iodide prescribed or administered

Condition	Responses, n (N=3) ^a
Pseudomonas of the nails ^b	1
Onychomycosis & mold in nails ^b	1
No Response	1

^aOut of 4 respondents, 3 reported prescribing or using thymol iodide.

^bPseudomonas of nails and onychomycosis & mold in nails not nominated.

Table 13. Reasons for using compounded thymol iodide

Reason	Responses, n (N=3) ^{a,b}
Commercial product not available in desired dosage form, strength or combination	1
Patient allergies prevent use of commercial products	0
Patient conditions prevent use of commercial products	1
No commercial products	2

^aOut of 4 respondents, 3 reported prescribing or using thymol iodide.

^bSome respondents reported more than one reason for using compounded thymol iodide.

Table 14. Use of non-patient-specific compounded thymol iodide

Do you stock non-patient-specific compounded thymol iodide at your practice?	Responses, n (N=3) ^a
Yes	0
No	2
No response	1

^aOut of 4 respondents, 3 reported prescribing or using thymol iodide.

CONCLUSION

Thymol iodide was nominated for inclusion on the 503B Bulks List as an absorbent and protective agent with antimicrobial properties via the topical ROA. Thymol iodide is not available in the nominated dosage form and ROA in any of the national medical registries searched. Thymol iodide is available as various OTC topical dosage forms in the US.

From the literature, topical thymol is used in combination with other APIs such as chlorhexidine for dental procedures as an oral antiseptic. Other indications include aiding in treatment of chronic paronychia, promoting episiotomy healing, and pleurodesis. From the interviews conducted, most SMEs were not familiar with and did not use thymol iodide. Thymus oil has broad-spectrum antimicrobial properties and when iodinated, there could be some absorbent capacity that could be useful for wound healing such as patients with leg ulcers, decubiti, or bad intertrigo. Also, thymol can be used as a mouth wash or in surgery to disinfect a site.

From the survey responses, 3 out of 4 respondents used thymol iodide. The only indications respondents used compounded thymol iodide for were pseudomonas of nails and onychomycosis and mold in nails. Lack of commercial products in an appropriate dosage form, strength or combination, patient conditions preventing use of commercial products, or no commercially available products with thymol iodide were the reasons given for using the compounded thymol iodide product over an FDA-approved product. Zero respondents reported stocking compounded thymol iodide.

REFERENCES

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3. Levac D, Colquhoun H, O'Brien KK. Scoping studies: Advancing the methodology. *Implementation Science*. 2010;5(1).
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5. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Med Res Methodol*. 2018;18(1):143-143.

APPENDICES

Appendix 1. Search strategies for bibliographic databases

MEDLINE search strategy

- Platform: Ovid
- Years searched: Ovid MEDLINE and epub ahead of print, in-process and other non-indexed citations and daily 1946 to December 20, 2019
- Date last searched: December 22, 2019
- Limits: Humans (search hedge); English language
- Number of results: 277

1	thymol/	2011
2	thymol.tw.	2708
3	thymoliodide.tw.	0
4	bithymol diiodide.tw.	0
5	bithymoldiiodide.tw.	0
6	diiododithymol.tw.	0
7	dithymol diiodide.tw.	1
8	dithymoldiiodide.tw.	0
9	iodo thymol.tw.	1
10	iodothymol.tw.	13
11	iodo hydromol.tw.	0
12	iodohydromol.tw.	0
13	annidalin.tw.	0
14	aristol.tw.	5
15	iodistol.tw.	0
16	iodostol.tw.	0
17	iosol.tw.	0
18	iothymol.tw.	0
19	lothymol.tw.	0
20	thymiode.tw.	0

21	thymiodol.tw.	0
22	thymodin.tw.	1
23	thymotol.tw.	0
24	or/1-23	3399
25	drug administration routes/	5605
26	administration, topical/	37797
27	administration, cutaneous/	21557
28	administration, intravaginal/	4734
29	administration, mucosal/	247
30	administration, rectal/	2504
31	topical\$.tw.	101568
32	cutaneous\$.tw.	147026
33	transdermal\$.tw.	14055
34	intravaginal\$.tw.	5448
35	vaginal\$.tw.	96972
36	mucosal\$.tw.	116615
37	rectal\$.tw.	85209
38	dosage forms/	5971
39	exp colloids/	122651
40	emulsions/	17417
41	gels/	28391
42	suspensions/	7637
43	liniments/	122
44	ointments/	12696
45	powders/	13497
46	suppositories/	3907

47	vaginal creams, foams and jellies/	1254
48	skin cream/	926
49	pharmaceutical solutions/	3290
50	drug compounding/	21558
51	emulsion?.tw.	31487
52	nanoemulsion?.tw.	2522
53	suspension?.tw.	105662
54	liniment?.tw.	141
55	ointment?.tw.	11577
56	salve?.tw.	336
57	paste?.tw.	11917
57	paste?.tw.	11917
58	unguent\$.tw.	110
59	lotion?.tw.	2230
60	cream?.tw.	18290
61	powder?.tw.	64188
62	suppositor\$.tw.	4342
63	varnish\$.tw.	3036
64	or/25-63	910302
65	drug therapy/	30272
66	exp anti-infective agents, local/	228081
67	antifungal agents/	56631
68	drug effects.fs.	2931056
69	drug therapy.fs.	2165840
70	administration & dosage.fs.	1383167
71	tu.fs.	2177114

72	antisept\$.tw.	8646
73	anti sept\$.tw.	182
74	antiinfect\$.tw.	706
75	anti infect\$.tw.	5972
76	antibact\$.tw.	70725
77	anti bact\$.tw.	3345
78	antimicrob\$.tw.	153912
79	anti microb\$.tw.	3963
80	antifung\$.tw.	47540
81	anti fung\$.tw.	2211
82	therap\$.tw.	2664073
83	treat\$.tw.	5283398
84	or/65-83	9696409
85	and/24,64,84	429
86	exp animals/ not humans/	4654789
87	85 not 86	328
88	limit 87 to english language	277

Embase search strategy

- Platform: Elsevier
- Years searched: 1947 to present
- Date last searched: December 22, 2019
- Limits: Humans (search hedge); English language; Publication type: article, article in press, conference abstract, conference paper, data papers, erratum, letter, note
- Number of results: 305

1	thymol'de	5309
2	thymol':ti,ab,tn	4860
3	thymoliodide':ti,ab,tn	0
4	bithymol diiodide':ti,ab,tn	0
5	bithymoldiiodide':ti,ab,tn	0
6	diiiododithymol':ti,ab,tn	1
7	dithymol diiodide':ti,ab,tn	3
8	dithymoldiiodide':ti,ab,tn	0
9	iodothymol':ti,ab,tn	21
10	iodo hydromol':ti,ab,tn	0
11	iodohydromol':ti,ab,tn	0
12	annidalin':ti,ab,tn	0
13	aristol':ti,ab,tn	10
14	iodistol':ti,ab,tn	0
15	iodostol':ti,ab,tn	0
16	iosol':ti,ab,tn	0
17	iothymol':ti,ab,tn	0
18	lothymol':ti,ab,tn	0
19	thymiode':ti,ab,tn	0
20	thymiodol':ti,ab,tn	0
21	thymodin':ti,ab,tn	1
22	thymotol':ti,ab,tn	0

23	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22	6760
24	drug administration route'/de	7723
25	rectal drug administration'/de	8616
26	topical drug administration'/exp	110117
27	cutaneous drug administration'/de	582
28	intravaginal drug administration'/de	6462
29	mucosal drug administration'/de	403
30	transdermal drug administration'/de	8792
31	topical*':ti,ab	144501
32	cutaneous*':ti,ab	211252
33	transdermal*':ti,ab	20539
34	intravaginal*':ti,ab	7315
35	vaginal*':ti,ab	151835
35	vaginal*':ti,ab	151835
36	mucosal*':ti,ab	165820
37	rectal*':ti,ab	135143
38	drug dosage form'/exp	413775
39	cream'/de	9038
40	gel'/exp	71368
41	liniment'/de	247
42	lotion'/de	2778
43	ointment'/exp	18238
44	paste'/de	2464
45	pomade'/de	79
46	powder'/exp	34295
47	salve'/de	166

48	suppository'/de	5978
49	suspension'/exp	105655
50	varnish'/de	598
51	cream\$:ti,ab	28690
52	emulsion\$:ti,ab	42988
53	liniment\$:ti,ab	230
54	lotion\$:ti,ab	3905
55	ointment\$:ti,ab	21122
56	paste\$:ti,ab	14386
57	pomade\$:ti,ab	138
58	powder\$:ti,ab	81821
59	salve\$:ti,ab	468
60	suppositor*':ti,ab	7029
61	suspension\$':ti,ab	140560
62	varnish*':ti,ab	3291
63	unguent*':ti,ab	239
64	#24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63	1437521
65	drug therapy'/de	693324
66	anti-infective therapy'/de	334
67	antimicrobial therapy'/exp	216832
68	drug dose':lnk	619974
69	drug administration':lnk	1699955
70	drug therapy':lnk	3806966
71	antisept*':ti,ab	12309
72	anti sep*':ti,ab	289

73	anti infect*':ti,ab	8795
74	antiinfect*':ti,ab	1470
75	antibact*':ti,ab	99143
76	anti bact*':ti,ab	5582
77	antimicrob*':ti,ab	206211
78	anti microb*':ti,ab	6644
79	antifung*':ti,ab	66716
80	anti fung*':ti,ab	4021
81	therap*':ti,ab	4013225
82	treat*':ti,ab	7661466
83	#65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82	11837500
84	#23 AND #64 AND #83	532
85	[animals]/lim NOT [humans]/lim	5966287
86	#84 NOT #85	412
87	#86 AND ([article]/lim OR [article in press]/lim OR [conference abstract]/lim OR [conference paper]/lim OR [data papers]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim)	350
88	#86 AND ([article]/lim OR [article in press]/lim OR [conference abstract]/lim OR [conference paper]/lim OR [data papers]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim) AND [english]/lim	305

Appendix 2. Survey instrument

Welcome. We want to understand your clinical use of compounded thymol iodide. Your feedback will help the Food and Drug Administration (FDA) develop a list of drugs that can be used in compounding by 503B outsourcing facilities. Your anonymous responses will be shared with the FDA. The time required to complete this survey is approximately 10-15 minutes.

If you have additional questions or concerns about this study, please email:
compounding@rx.umaryland.edu.

If you have questions about your rights as a research subject, please contact HRPO at 410-760-5037 or hrpo@umaryland.edu.

Thank you,

Dr. Ashlee Mattingly,
Principal Investigator
The University of Maryland School of Pharmacy

An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

OMB Control No. 0910-0871
Expiration date: June 30, 2022

1. How familiar are you with the following terms?

	Very familiar	Somewhat familiar	Not familiar
Compounded drugs (medications prepared to meet a patient-specific need)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
503A Compounding pharmacy (a pharmacy that prepares compounded medications prescribed by practitioners to meet a patient-specific need)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
503B Outsourcing facility (a facility that compounds larger quantities without the receipt of a patient-specific prescription)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

2. Do you prescribe or administer thymol iodide to your patients?

- Yes
- No

3. I prescribe or administer thymol iodide for the following conditions or diseases (please list): _____

4. I use thymol iodide with my patients as the following: (check all that apply)

- FDA-approved drug product
- Compounded drug product
- Over-the-counter drug product
- Dietary supplement (e.g. vitamin or herbal supplement sold in retail)
- Other (please describe) _____

5. I use compounded thymol iodide because: (check all that apply)

- Commercial products are not available in the dosage form, strength, or combination I need. (please explain) _____
- Patient allergies prevent me from using commercially available products. (please explain) _____
- Patient conditions prevent me from using commercially available products. (please explain) _____
- There are no commercially available products containing thymol iodide.
- Other (please explain) _____

6. Do you stock non-patient-specific compounded thymol iodide at your practice?
- Yes
 - No
 - I'm not sure
7. I obtain compounded thymol iodide from the following: (check all that apply)
- Compound myself at my practice
 - Have the product compounded by an in-house pharmacy
 - Purchase, or have a patient purchase, from a compounding pharmacy
 - Purchase, or have a patient purchase, from an outsourcing facility
 - Other (please explain) _____
8. What is your practice setting? (check all that apply)
- Physician office/private practice
 - Outpatient clinic
 - Hospital/health system
 - Academic medical center
 - Emergency room
 - Operating room
 - Other (please describe) _____
9. What degree do you hold? (check all that apply)
- Doctor of Medicine (MD)
 - Doctor of Osteopathic Medicine (DO)
 - Doctor of Medicine in Dentistry (DMD/DDS)
 - Doctor of Pharmacy (PharmD) or Bachelor of Science in Pharmacy (BS Pharm)
 - Naturopathic Doctor (ND)
 - Nurse Practitioner (NP)
 - Physician Assistant (PA)
 - Other (please describe) _____

Appendix 3. Survey distribution to professional associations

Specialty	Association^a	Agreed/Declined, Reason for Declining
Allergy/Immunology	American Academy of Allergy, Asthma, and Immunology (AAAAI)	Declined – survey not approved
Anesthesia	American Society of Regional Anesthesia and Pain Medicine (ASRA)	Declined – failed to respond
	Society for Ambulatory Anesthesia (SAMBA)	Declined – failed to respond
	Society for Neuroscience in Anesthesiology and Critical Care	Declined – failed to respond
Critical Care	Critical Care Societies Collaborative	Declined – failed to respond
Dentistry & Oral Medicine	Academy of General Dentistry (AGD)	Declined – provided interview referrals
	American Dental Association (ADA)	Declined – failed to respond
Dermatology	American Academy of Dermatology (AAD)	Agreed
	American Osteopathic College of Dermatology (AOCD)	Declined – not interested
Endocrinology	The Endocrine Society (ENDO)	Agreed
	Pediatric Endocrine Society	Agreed
Gastroenterology	American Gastroenterological Association (AGA)	Declined – failed to respond
	Obesity Medicine Association (OMA)	Declined – did not have anyone to contribute to research
Hematology	American Society of Hematology (ASH)	Declined – does not distribute surveys
Infectious Disease	American Academy of HIV Medicine (AAHIVM)	Declined – failed to respond
Medicine	American Medical Association (AMA)	Declined – failed to respond

Naturopathy	American Association of Naturopathic Physicians (AANP)	Agreed
	The Oncology Association of Naturopathic Physicians (OncANP)	Agreed
Nephrology	American College of Clinical Pharmacists: Nephrology Practice Network	Agreed
	American Society of Nephrology	Declined – provided interview referrals
Nutrition	American Society for Parenteral and Enteral Nutrition (ASPEN)	Declined – provided interview referrals
Obstetrics and Gynecology	American Gynecological and Obstetrical Society (AGOS)	Declined – failed to respond
	Nurse Practitioners in Women’s Health	Agreed
Ophthalmology	American Academy of Ophthalmology (AAO)	Agreed
Otolaryngology	American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS)	Declined – survey not approved
Pain Management	American Academy of Pain Medicine (AAPM)	Declined – survey not approved
	American Academy of Physical Medicine and Rehabilitation	Declined – failed to respond
Pediatrics and Neonatology	American Academy of Pediatrics (AAP)	Agreed
Primary Care	American College of Physicians (ACP)	Declined – failed to respond
Psychiatry	American Academy of Clinical Psychiatrists	Declined – failed to respond
	American Association for Geriatric Psychiatry	Declined – failed to respond
Rheumatology	American College of Rheumatology (ACR)	Agreed

Surgery	Ambulatory Surgery Center Association (ASCA)	Agreed
	American Academy of Orthopaedic Surgeons (AAOS)	Declined – no interest in participation from members
	American Association of Hip and Knee Surgeons (AAHKS)	Declined – only send surveys from members
	American College of Surgeons (ACS)	Agreed
	American Society for Metabolic and Bariatric Surgery (AMBS)	Declined – only send surveys from members
	The Association of Bone and Joint Surgeons	Declined – failed to respond
	Physician Assistants in Orthopaedic Surgery	Declined – failed to respond
	Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)	Declined – failed to respond
	Society of Gynecologic Surgeons (SGS)	Declined – policy limits number of surveys per year and do not have a method to identify if any of the SGS members are using ipamorelin
Toxicology	American Academy of Environmental Medicine (AAEM)	Declined – failed to respond
Urology	Sexual Medicine Society of North America (SMSNA)	Agreed

^aAssociations that declined in Year 1 were not contacted in Year 2.