Content Analysis of Complementary and Alternative Medicine Literature in the Journal of the Philippine Dermatological Society

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Background: Complementary and alternative medicine (CAM) is a popular treatment option among patients. There is a need to assess the content of published local literature on complementary and alternative medicine in dermatology in the Journal of the Philippine Dermatological Society (JPDS) to provide evidence for its integration into clinical practice and to guide future research .

Objective: To analyze the content of published literature on complementary and alternative medicine published in the JPDS

Method: We screened the titles and abstracts of all published articles in the JPDS from 1992-2017 and included articles on any aspect of complementary and alternative medicine. We extracted relevant characteristics such as study design, disease, type and details of CAM therapies, from the included articles. We summarized data using descriptive statistics for continuous data, and frequency distribution for ordinal data.

Results: CAM articles accounted for 4% of all published articles in the JPDS over the past 25 years of its existence. Most were RCTs (22%) (mean size=69), with the greatest number being on herbal medicine (66%), and for the treatment of infections, infestations and bites (46%). Majority of articles were primarily authored by resident trainees (87%) and the most common institutional affiliation was UP-PGH (24%). Among the herbal articles, the most common herb family was Fabaceae (9%), while coconut had the highest number of articles. Leaves were the most common plant part used (40%), and creams were the predominant type of formulation (29%). Other CAM interventions included were animal products, dietary supplements, and lifestyle modification.

Conclusion: The poor representation of CAM in the JPDS may reflect the lack of integration of this field in the local practice of dermatology. There is a need to increase awareness and gather more evidence on the application of CAM in the maintenance of healthy skin as well as prevention and treatment of skin diseases.

Key words: content, complementary therapies, complementary medicine. alternative medicine, traditional medicine, herbal, Journal of the Philippine Dermatological Society

INTRODUCTION

omplementary and alternative medicine (CAM) is a popular treatment option among patients, and is often perceived to be a safer and more holistic approach to treating disease. In a survey of 552 dermatology outpatients in Turkey, the prevalence of CAM use was 16.8%.¹ In a survey of 148 dermatologists from the Philippine Dermatological Society (PDS), most had adequate knowledge (59%) and a positive attitude about CAM (81%). Most respondents reported patient interest in CAM (71%) and recommended CAM (87%) for skin conditions.²

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Source of funding: Philippine Dermatological Society Research Grant Conflict of interest: none Corresponding author: Rowena Natividad S. Flores-Genuino, MD, MSc, FPDS Email: rfgenuino@post.upm.edu.ph However, it is one of the less studied areas of medicine and not sufficiently covered in textbooks or training programs. Although most of the treatments are derived from natural products or based on traditional use and cultural beliefs and practices, its efficacy and safety is still unclear.

A systematic review of 57 trials and 3 meta-analyses on the most commonly studied complementary and alternative medicine therapies in plaque psoriasis found that *Indigo naturalis*, curcumin, dietary modification, fish oil, meditation, and acupuncture had the most robust evidence of efficacy.³ Another systematic review of 70 RCTs in mild-to-moderate atopic dermatitis showed some level I evidence to support the use of acupuncture and acupressure, stress-reducing techniques such as hypnosis, massage, and biofeedback, balneotherapy, herbal preparations (with many important caveats), certain botanical oils, oral evening primrose oil, vitamin D supplementation, and topical vitamin B12.⁴

However, in a narrative review of Cochrane systematic reviews, the use of 10 integrative practices that have recently been incorporated into Brazil's public health care system does not seem to be supported by evidence, except for some specific uses of apitherapy (honey for burn wounds and for acute coughs and bee venom for allergic reactions to insect stings).⁵

Recently, akapulko (Cassia alata), previously recommended by the Philippine Department of Health for the treatment of tinea versicolor in the 1990s, was delisted from the 2017 Philippine National Drug Formulary (PNDF) since it had no certificate of product registration (Personal communication, Dr. Cecilia Maramba-Lazarte). In general, there seems to be a lack of firm clinical evidence that could support the use of herbal medicine and other traditional and alternative health care modalities for skin diseases. This is despite the Traditional and Alternative Medicine Act (Philippine Republic Act 8423) of 1997,⁶ which defined "traditional and alternative health care" as "the sum total of knowledge, skills and practices on health care, other than those embodied in biomedicine (or western medicine), used in the prevention, diagnosis and elimination of physical or mental disorder." Alternative health care modalities include "other forms of non-allopathic, occasionally non-indigenous or imported healing methods, though not necessarily practiced for centuries nor handed down from one generation to another" such as reflexology, acupressure, chiropractics, and nutritional therapy.⁶

There are no systematic reviews on the use of traditional and alternative medicine in dermatology in the Philippines that may be used to support its integration into the national health care system. The Journal of the Philippine Dermatological Society (JPDS) is the official publication of the official dermatological society since 1992 and serves as a leading source of information to guide the practice of dermatology in the Philippines. There is a need to assess the scope and breadth of the JPDS in the field of complementary and alternative medicine. This will guide dermatologists and their patients in the rational and evidencebased use of complementary and alternative therapies in preventing and treating skin disease. Future directions of research in this field can also be elucidated based on this review.

OBJECTIVE

To analyze the content of complementary and alternative medicine literature published in the JPDS from 1992 to 2017

METHODS

- 1. Study design:
- Journal review 2. Study population/Sampling/Sample size: All articles published in the JPDS from 1992-2017
- 3. Article eligibility

We included all articles on complementary and alternative medicine published in the JPDS from 1992-2017. We included all types of articles, whether original research (primary or secondary), or non-research (narrative reviews, critical appraisals)

4. Searching for eligible articles

We scanned the table of contents of all available issues of the JPDS and screened potentially relevant titles and

abstracts. The full texts of those that seemed to fulfill the inclusion criteria were retrieved and assessed for eligibility.

5. Data collection

We used a pre-tested data collection form to extract the following information from the full text of each article: General data: Study ID (Author's last name and Year published), citation, professional status of main author, institutional affiliation, study design, study setting, ethical approval, source of funding, duration of follow-up Study details: study population, sample size, disease, type of CAM, details of CAM intervention, brand name/manufacturer, dosage, duration of treatment

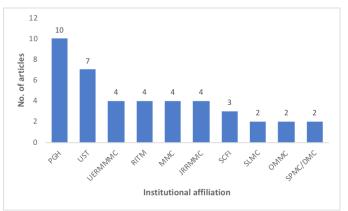
6. 7. Data analysis:

Data was entered into Microsoft Excel [2016]. Descriptive analysis was performed for continuous data, and frequency distribution for ordinal data was computed.

RESULTS

Out of 51 issues of JPDS over a 25-year span (1992-2017), we scanned the titles and/or abstracts of 1040 articles and after retrieving the full reports of potentially relevant articles, we assessed 42 articles to be eligible for this review (42/1040, 4%). Details of included articles are in Appendix 1 and 2.

Majority had resident trainees (87%) as main authors and only 13% were consultants. The top institutional affiliations of the CAM studies were the University of the Philippines-Philippine General Hospital (24%), and Santo Tomas University Hospital (17%) (Fig. 1).





The CAM articles were published from 1994 to 2017, with two peaks (n=5) in 2008 and 2013. The number of articles doubled from 1990s (10) to 2000s (20). However, it remained almost the same from 2000s to 2010s (18, up to 2017) (Fig.2).

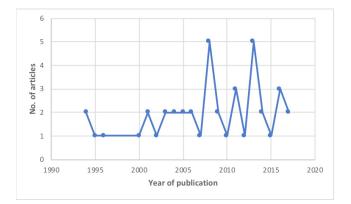


Figure 2. Frequency distribution of CAM articles as to year of publication (N=42)

Majority of the articles were primary (83%) or secondary research (2%) studies while the rest were non-research (15%). Majority of the primary research were RCTs (42%) and in-vitro (15%). The non-research articles were critical appraisal articles (9%) or narrative reviews (6%) (Fig. 3).

Note: N=53 since some articles were hybrids of 2 or more different study designs

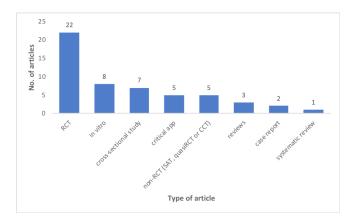


Figure 3. Frequency distribution of CAM articles as to type of article

Among the 22 RCTs, majority (19) compared an alternative intervention with standard of care, while a few were placeboor vehicle-controlled (6). No RCT tested an intervention as an adjunct to standard treatment versus standard treatment alone. Mean sample size was 69 (range 8, 272). The smallest-sized RCT (N=8) was an intra-individual comparison of topical niacinamide cream with placebo and sunblock to prevent UVB-induced erythema.⁷ The largest RCT (N=272) compared the efficacy of topical aromatic oils to lindane shampoo in the treatment of head lice in orphanages.⁸ It was one of only five funded studies and one of three that received funding from PCHRD. One study reported receiving funding from the Philippine Dermatological Society while another, from a commercial company (Johnson & Johnson, Philippines).

The most common general topic of CAM intervention was herbal medicine (29/44, 66%), followed by animal products (6/44, 14%), and dietary supplements (4/44, 9%) (Fig. 4).

Note: N=44 since some articles had more than 1 topic

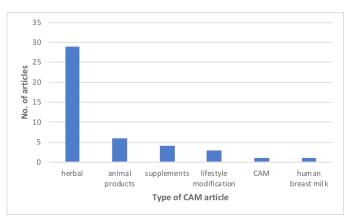


Figure 4. Frequency distribution of CAM articles as to general topic

The disease category or topic studied in almost half of the articles were infections, infestations and bites (31/67, 46%), while eczemas/allergies were studied in 10/67 or 15% of articles (Fig. 5).

Note: N=67 since some articles had more than one disease category or topic

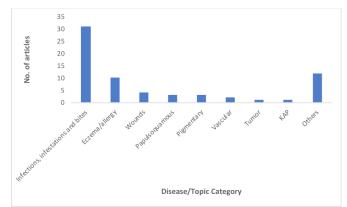


Figure 5. Frequency of distribution of CAM articles as to disease category

For the herbal articles (n=29), there were a total of 37 herb families studied. The most commonly studied herbs belonged to the family Fabaceae (12/136, 9%) specifically akapulko (6/136, 5%) and kakawate (4/136, 3%). In second place were Lamiaceae (10/136, 7%), with lavender and rosemary (2/136, 2% each) and Myrtaceae (10/136, 7% each). For Arecaceae, the most common

herb was coconut (7/136, 6%); and for Myrtaceae, guava (4/136, 3%). The third most common herb family studied in the articles was Solanaceae (7/136, 5%), mainly siling labuyo (2/136, 2%) (Fig. 6).

Note: N=136 since some studies had more than one family of herb

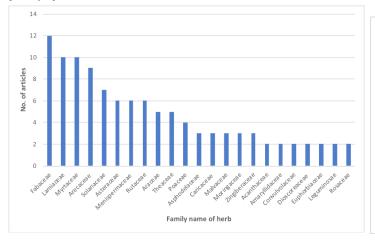
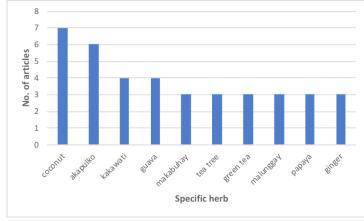
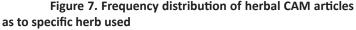


Figure 6. Frequency distribution of herbal CAM articles as to family name of herb

The most common herb studied was coconut (7), followed by akapulko (6), kakawati (4) and guava (4) (Fig. 7).





Majority of studies used single plants (17) while 4 studies used compounds that were a mixture of two or more plants (Francisco-Diaz 2004; De las Alas 2013; Ong-Salvador 2000; Perez-Chua 2012). Two studies tested two (Lo-Letran 1995) and three (Joven 2003) individual plant species, respectively. Five studies used single compounds: monolaurin 2% (gel, Abraham 2001; cream, Dim-Jamora 2006), capsaicin 50% and 75% ointment (Banzon 2008), capsaicin 0.025% cream (De Leon-Godinez 2011) , tannin 40% cream (Ty 2003). The ethnopharmacologic review studied 58 unique identifiable plants and 4 animal products (SaludGnilo 2014). The most common parts of the plant used were the leaves (46/116, 40%), roots (14/116, 8%) and bark (9/116, 7%) (Fig. 8). All herbal products were topically applied and most common types of herbal preparations were creams (10/35, 29%), ointment (6/35, 17%) and oil (5/35, 14%) (Fig. 9).

Note: N=116 since some studies included more than one plant part

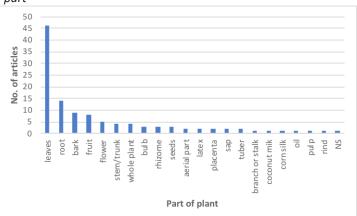


Figure 8. Frequency distribution of CAM herbal articles as to part of plant

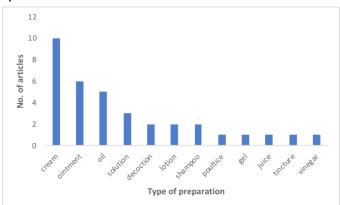


Figure 9. Frequency distribution of CAM herbal articles as to type of preparation

Among the non-herbal CAM articles (n=13), a variety of animal products, lifestyle modification, oral dietary supplements, and topical interventions were given. Novel topical interventions for atopic eczema such as human breast milk and probiotics were studied in a critical appraisal article and an RCT, respectively. Lifestyle modification in the form of weight loss through lowcalorie diet for psoriasis was the topic in two critical appraisal articles. The use of glutathione supplements in skin whitening and rejuvenation was the topic in three articles by the same author: cross-sectional survey and key informant interview, systematic review, critical appraisal article and narrative review. A cross-sectional survey explored the knowledge, attitude and practices of dermatologist members and trainees of the Philippine Dermatological Society,

DISCUSSION

CAM articles made up only 4% of all published articles in the JPDS over the past 25 years of its existence. The most common study design was RCTs (22%) (mean size=69), with the greatest number being on herbal medicine (66%), and for the treatment of infections, infestations and bites (46%). Majority of articles were primarily authored by resident trainees (87%) and the most common institutional affiliation was UP-PGH (24%). Among the herbal articles, the most common herb family was Fabaceae (9%). Leaves were the most common plant part used (40%), and creams were the predominant type of formulation (29%).

The trend of CAM publication in the JPDS showed that the number of articles doubled from the 1990s to the 2000s but plateaued in the 2010s. The RCTs were mostly small-sized, and mainly compared the test intervention as an alternative treatment to standard or accepted drug. All RCTs utilized topical applications and may reflect the unique accessibility of skin lesions for local interventions. Limited evidence on safety of CAM interventions, especially oral dietary supplements and herbs, and safety concern among human participants may also explain why no RCTs tested oral interventions. It was noted that there was no study that used an intervention as a complementary or adjunct treatment to standard of care.

Our results are consistent with a previous systematic review on published herbal interventions in the ASEAN Plus Six countries, wherein Thailand had the most number (26/71), and the Philippines had the least number of herbal RCTs (1/71) indexed in major electronic databases.⁹ This lone herbal RCT from the Philippines was not in the field of dermatology: it was on the use of ampalaya in diabetes mellitus. Although majority of articles were RCTs, most were small-sized (less than 100), and be due to lack of funding. Being small-sized, these were likely pilot trials that were not followed up with larger confirmatory trials. This shows the lack of continuity in the herbal research agenda, which may be due to the fact that main authors were mostly resident trainees and not the consultant faculty. It is noteworthy, however, that two RCTs, conducted 12 years apart, tested the same intervention (topical aromatic oils) but against a different standard of care (lindane shampoo in 2000, and permethrin shampoo in 2012). There were only a few studies that declared funding source (PCHRD), despite herbal medicine being included in the Philippine national health research agenda since the 1990s. The establishment of the National Integrated Research Program on Medicinal Plants (NIRPROMP) in 1987 in UP Manila, may explain the greater number of CAM studies in UP-PGH. It was this collaboration that gave birth to the inclusion of akapulko, an antifungal lotion, as one of the ten DOH-recommended medicinal plants.

The skin diseases covered by majority of the articles were infections, infestations and bites. This is congruent with the top 10 diagnoses at the training institutions of the Philippine Dermatological Society (PDS) in 2017 where the top 2 (dermatophytosis, 7.8%), top 5 (scabies, 4.5%) and top 10 (verruca

vulgaris, 3.4%) diagnoses in new and returning cases (N=46,109) were all infections or infestations (PDS-Health Information System, PDS-HIS). Eczemas and inflammatory skin diseases which were the second most common topic in the JPDS articles (15%) occupied six of the top ten diagnoses in PDS-HIS (allergic contact dermatitis, seborrheic dermatitis, atopic dermatitis, lichen simplex chronicus, psoriasis, and irritant contact dermatitis). Surprisingly, acne was the top diagnosis in the PDS-HIS 2017 data and yet was only discussed in one review article in JPDS on the role of diet in acne.

The most commonly studied family of herbs was Fabaceae (mainly akapulko) while the herb with most number of articles is the coconut. Akapulko is one of the ten medicinal plants recommended by the Department of Health in the 1990s although it is not currently being marketed. Coconut is a locally sustainable crop, and its oil has been used for centuries as a moisturizer. It is also a popular ingredient in many cosmetics and toiletries. Cream preparation was used in majority of studies probably due to its more elegant feel and cosmetic acceptability, especially in tropical and humid climate of the Philippines. The use of leaves as the raw material of the medicinal products in majority of the articles highlights the sustainability of herbal medicine.

Among the dietary supplements that were included mostly in reviews, glutathione was featured in three articles in 2002, 2008 and 2009. Soon after, in 2011, the Philippine FDA banned its use as intravenous drip for skin whitening.¹⁰ However, lifestyle modification, such as diet and weight loss interventions, was only tackled in the form of critical appraisal articles of RCTs, which aimed to apply best current evidence to specific clinical scenarios. Obesity is a rising epidemic that is a risk factor not only for the so-called 'lifestyle diseases" such as diabetes, hypertension and dyslipidemia, but also for psoriasis. There were also some novel interventions tested for efficacy in RCTs and included human breast milk and topical probiotics for atopic eczema, and topical niacinamide cream for photoprotection, but these were small to medium-sized trials that need to be further validated. Notably, there were no articles on acupuncture, traditional Filipino, Chinese and Ayurvedic medicine, which are widely practiced by our diverse and multi-ethnic population.

The field of CAM is poorly represented in the JPDS, and the initial upward trend in the 2000s seem to have plateaued in the last decade. The most common study design was RCTs, with herbal medicine as the type of CAM in majority of articles, mainly for the treatment of infections, infestations and bites. Majority of CAM literature was authored by resident trainees and the most common institutional affiliation was UP-PGH. Among the herbal articles, the most common herb family was Fabaceae, with coconut as the most widely studied. Leaves were the most common plant part used, often in topically applied cream formulations.

LIMITATIONS

We limited our analysis to articles published in the Journal of the Philippine Dermatological Society but a more comprehensive bibliometric review can be done. The scope can be widened to include all major Philippine journals that publish topics in dermatology or CAM. We did not analyze the level or quality of evidence from the articles since this was not part of our objectives, but this would be an important step in formulating practice guidelines for both clinicians and policy makers.

CONCLUSION

The poor representation of CAM in the JPDS may reflect the lack of integration of this field in the local practice of dermatology. There is a need to increase awareness and gather more evidence on the application of CAM in the maintenance of healthy skin as well as prevention and treatment of skin diseases.

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RECOMMENDATIONS

Systematic reviews on the different popular CAM remedies on common skin diseases should be done to determine level of evidence and to identify research gaps. Efficacy and safety should be established through RCTs while pharmacovigilance and post-marketing surveillance should be performed to monitor safety.

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Appendix 1

Characteristics of Included Herbal CAM Articles (N=29)

| Study ID | Institution Of Main Author | Study Design | Disease/ Topic | Herb/Part/ Preparation | Sample Size | Study Setting & Study Population | Duration Of Follow-Up | Ethical Approval | Study Funding |
|----------------------------------|-------------------------------|---|-------------------|--|----------------|---|-------------------------------|---------------------|--------------------|
| | | RCT | | | 45 | | 5 min | | |
| 1. Abraham 2001 ¹¹ | MMC | In vitro | Hand bacteria | Monolaurin 2% gel (From coconut kernel) | NA | Nurses at tertiary hospital | pital , incubation | Y | Y, Johnson & |
| 2001 | | Cross-sectional (patch testing) | | Cocos nucifera (L.) | 15 | nospital | 4 days | n Y & Joł | Johnson |
| 2. Angeles 2004 ¹² | UERMMMC | RCT, active- and placebo-controlled (3-arm) | UVB erythema | Green tea leaf extract 10% cream (Tegreen capsule, Pharmanex, 250 mg capsule) containing 4.55 mg/ cm catechins <i>Camellia sinensis</i> (L.) Kuntze | 30 | Healthy human volunteers with Fitzpatrick Skin Type III/IV | 24 hrs. for MED reading | Y | NS |
| 3. Banzon 2008 ¹³ | RITM | RCT, placebo- controlled | Pain | Capsaicin 50% and 75% ointment (Siling labuyo/ <i>Capsicum frutescens</i> (L.) | 85 | Dermatology OPD, RITM Adults aged 18-60 years old | 9 days | NS | NS |

39.

| 4. Buensalido 2011 ¹⁴ | ММС | RCT Cross-sectional (Patch test) | Dermato- phytoses (tinea corporis) | Papaya fruit latex 1.5% cream (<i>Carica papaya</i> L.) | 60 | NS Age not stated | 6 mos. | Y | N |
|--|------------------------------------|--|--|--|------------------|--|---------|----|-------------|
| 5. Cabillos 2003 ¹⁵ | ММС | RCT, vehicle- controlled | Molluscum contagiosum | Green tea extract 5% Cream <i>Camellia sinensis</i> | 69 | Makati Medical Center OPD Children and young adults | NS | Y | NS |
| 6. Caumban- King 1996 ¹⁶ | STUH | ССТ | Palmar or plantar hyperhidrosis | Black tea aqueous solution (Lipton black tea bags) Camellia sinensis | 42 | 13-32 (mean 22.5) | 1 wk. | NS | NS |
| 7. Cue 2010 ¹⁷ | STUH | RCT | Dermato- phytoses (tinea corporis and cruris) | Lemongrass 10% oil Cymbopogon citratus | 96 | Not stated 2-70 years old | 4 wks. | Y | N |
| 8. De las Alas 2013 ¹⁸ | UP-PGH | Case report | Reactive epidermal hyperplasia | Berberine, sitosterol, golden thread rhizome, Amur Cork- tree bark, Baical skullcap root, poppy capsule, and earthworm (Moist Exposed Burn Ointment) | 1 | 42 y.o./F | 2 wks. | NA | None |
| 9. De Leon- Godinez 2011 ¹⁹ | RITM | RCT Cross-sectional (patch test) | Mosquito bites | Capsaicin 0.025% cream (Siling haba/ Capsicum annuum var. longum) | 75 | Dermatology and Entomology Laboratory, RITM 18 to 60 years old | 1 mo. | NS | N |
| 10. Dim- Jamora ²⁰ | SCFI | RCT In vitro | Superficial bacterial skin infections | Monolaurin 2% cream (from coconut kernel) <i>Cocos nucifera</i> | 18 | 1 to 43 y.o. | 2 wks. | NS | NS |
| 11. Dofitas 2001 ²¹ | PGH | RCT | Tinea versicolor | Akapulko 50% lotion <i>Cassia alata</i> | 129 | Dermatology clinic of PGH 7-65 years old | NS | NS | Y, PCHRD |
| 12. Dumandan 2002 ²² | JRRMMC | Critical appraisal of an RCT | Tinea pedis | Tea tree oil 25% and 50% solution <i>Melaleuca alternifolia</i> | 1 RCT (N=158) | 14 y.o and older | 4 wks. | NS | NS |
| 13. Francisco- Diaz 2004 ²³ | Skin Cancer Foundation, Inc. | RCT, placebo- controlled | Melasma | Gigawhite 5%™ solution (Various - mallow, peppermint, primrose, lady's mantle, lemon balm, yarrow) | 28 | Makati Medical Center Adults | NS | NS | NS |
| 14. Guillano 2005 ²⁴ | Davao Medical Center (DMC) | RCT | Dermato- phytosis (tinea corporis and cruris) | Kakawati 50% ointment Gliciridia sepium | 40 | DMC dermatology clinic 7-79 years old | 4 wks. | NS | NS |
| 15. Hau 2008 ²⁵ | JRRMMC – | RCT In vitro | Dermato- phytosis (tinea corporis and cruris) | Ginger rhizome powder 25 mg/g cream Zingiber officinale | 24 | Not stated 12-70 years old | 8 wks. | NS | NS |
| 16. Joven 2008 ²⁶ | ммс | In vitro | Antimicrobial activity | Grapefruit/Citrus paradisi seeds; calamansi/ Citrofortunella microcarpa pulp; pomelo/Citrus grandis rind Alcoholic extract solution; Oils | NA | Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans | 48 hrs. | NS | NS |
| 17. Lagunzad 2013 ²⁷ | UERMMMC | RCT | Common warts | Apple cider vinegar (Bragg's™) | 27 | STUH- OPD | 5 wks. | Y | N |
| 18. Lo-Letran 1995 ²⁸ | STUH | In-vitro | Anti-microbial acrivity | Allium sativum/Garlic bulbs; Aloe vera leaves Poultice, infusion, extract in coconut oil | NA | 2-60 years old S. aureus, Klebsiella, E.coli, Proteus, Pseudomonas, Candida, Beta- hemolytic Streptococcus | 48 hrs. | NS | NA |
| | | | | | | | | | |

| 19. Naagas- Sarmiento 2013²⁹ 20. Ong- Salvador 2000⁸ | UERMMMC | RCT RCT In vitro | Seborrheic dermatitis Head lice | Guava extract 10% shampoo Psidiium guajava Lavender/Lavandula spp, rosemary/ Rosmarinus officinalis, eucalyptus Eucalyptus globulus / in sunflower/ Helianthus annuus oil | 45 272 | Dermatology clinic, UERMMMC 18-60 y.o. Selected orphanages in Metro Manila 6-15 y.o. | 4 mos. 1 yr. | Y | N Y, PCHRD |
|---|---------|--|---|--|---|---|-----------------|----|------------------|
| 21. Perez- Chua 2012 ³⁰ | STUH | RCT In vitro Cross-sectional (patch test) | Head lice | Lavender/Lavandula spp, rosemary/ Rosmarinus officinalis, eucalyptus Eucalyptus globulus / in sunflower/ Helianthus annuus oil | 154 | Community in Bulacan Children, adults, and elderly | 3 wks. | Y | N |
| 22. Salcedo- Rubio 1994 ³¹ | JRRMMC | SAT | Molluscum contagiosum | Garlic bulb cream (KYOLIC [®] Aged garlic extract capsules) Allium sativum | | Dermatology department 3-9 y.o. | 4 wks. | NS | Y |
| 23. Salud- Gnilo 2014 ³² | UP-PGH | Ethnopharmacologic survey | Various | 58 identified plants, 4 animal species | 28 folk healers & 174 community members | Samar Island Natural Park, 8 communities | 6 mos. | NS | N |
| 24. Sayo- Bondoc 2016 ³³ | ОММС | RCT | Localized pyoderma | Malunggay 15% ointment Moringa oleifera | 66 | Department of Dermatology, OMMC 6-15 y.o. | 4 mos. | Y | N |
| 25. Sembrano- Ilagan 1994 ³⁴ | STUH | CCT In-vitro | Bacterial skin infections | Tonkin seeds extract 10% cream (CMC-10) Ipomoea muricata | 95 | Outpatient Dept depressed areas of QC, Sampaloc District, Manila, Mandaluyong, Sapang Palay Mean 6-8 y.o | NS | NS | NS |
| 26. Sia 1994 ³⁵ | UP-PGH | Narrative review | Fungal infections, Wounds, Scabies | Akapulko Guava Makabuhay and 18 other plants | NA | NA | NA | NA | NA |
| 27. Sta. Ana 1995 ³⁶ | RITM | QuasiRCT | Prevention of mosquito bites | Tea tree 50% oil (Main Camp Pharmaceutical Grade, EuroChem) <i>Melaleuca alternifolia</i> | 20 | Entomology Section of RITM Healthy subjects | 8 hrs. | NS | NS |
| 28. Tavanlar- Amado 2014 ³⁷ | UERMMMC | RCT | Warts | Papaya latex extract cream (BlemishOFf Herbocautery cream) Carica papaya | 74 | Dermatology OPD, UERMMMC 5-70 y.o. | 6 mos. | Y | NS |
| 29. Ty 2003 ³⁸ | STUH | SAT | Tinea versicolor | 40% tannin cream (from calamansi pulp extract/ <i>Citrus</i> <i>microcarpa Bunge</i>) | 15 | 18-65 y.o. without dermatoses | 4 wks. | Y | NS |
| | | Cross-sectional (patch test) | | 20%, 40% and 80% tannin cream | 100 | 18-65 y.o. with tinea versicolor | 4 days | Y | NS |

Legend: MMC Makati Medical Center; RCT randomized controlled trial; N No; Y Yes; UERMMMC Univ. of the East-Ramon Magsaysay Memorial Medical Center; UVB Ultraviolet B; MED Minimal Erythema Dose; RITM Research Institute of Tropical Medicine; STUH Santo Tomas University Hospital; JRRMMC Jose R. Reyes Memorial Medical Center; PGH Philippine General Hospital; OMMC Ospital ng Maynila Medical Center; CCT controlled clinical trial; SAT single arm trial

Appendix 2 Characteristics of Included Non-Herbal CAM Articles (N=13)

| Study ID | Institution | Study Design | Disease/Topic | CAM intervention details | Sample size | Study Setting/ Population | Duration of ff-up | Ethical approval | Funding |
|--------------------------------------|-------------|--|--|---|--|--|--------------------------------|---------------------|---|
| 1. Abad-Venida 2011 ³⁹ | JRRMMC | Narrative review- summarized results of another review (Bowe 2010) | Acne | Diet -Dairy products -Chocolate -Vitamin A -Zinc -Low glycemic vs. carbohydrate- | 1 review (N=19 studies) (case series, cohorts, cross-sectional surveys, RCTs and nonRCTs) | NA | NA | NA | None; Author is a member of Galderma acne board |
| 2. Concha 2016 ⁷ | UP-PGH | RCT | Prevention of UVB-induced erythema | dense diet Niacinamide 4% cream (Skinceutique Philippines, FDA- approved) Applied 30 min prior to broadband UVB | N=8 | Healthy non-tanned volunteers | 24 hrs. | Y | Y, PDS |
| 3. Dellariarte 2017 ⁴⁰ | SCFI | Case report | Allergic contact | broadband UVB Bee propolis | N=1 | Patient with | NS | NA | None |
| 4. Dofitas | UP-PGH | Critical | dermatitis Photoaging | Natural marine | 3 RCTs (N not | plantar eczema NS | NS N | NA NS | |
| 200241 | | appraisal | Androgenic alopecia | complex PO Cartilaginous fish extract with | given) 1 RCT (N=40) | NS | | | |
| | | | Skin rejuvenation | silica PO Bee pollen | 5 case reports on allergies to | NS | | | |
| | | | Photoprotection | Vitamin E (1000 IU/2 g) + C (2-3 | bee pollen 2 RCTs (N=10; N=40) | NS | | | |
| | | | Photoprotection | g) PO Vitamin E 400 IU/ | 1 open RCT | NS | | | |
| | | | Nail quality | day PO x 6 mos. Calcium 1 g/day | (N=12) 1 RCT (N=683) | NS | | | |
| | | | Prevention of non-melanoma skin cancer | PO x 12 mos. Selenium 200 micrograms/day x 4.5 yrs. (mean) | 1 RCT (N=132) | Prior basal or squamous cell carcinoma | | | |
| | | | (NMSC) Psoriasis | Selenium PO 600 micrograms with or without Vitamin E x 12 wks. | 1 RCT (N=69) | Mod-to-severe plaque psoriasis | | | |
| | | | Atopic eczema | Selenium PO 600 micrograms x 12 | 1 RCT (N not given) | Moderate-to- severe atopic | | | |
| | | | Prevention of | wks. Beta-carotene 50 | 1 RCT | eczema Healthy male | | | |
| | | | NMSC Prevention of NMSC | mg x 12 yrs. Beta-carotene PO 50 mg/day x | (N=21,884) 1 placebo- controlled RCT | physicians Recent NMSC | | | |
| 5. Dofitas 2008 ⁴² | UP-PGH | 1. Cross sectional survey & KII | Skin whitening | 3-5 yrs. Glutathione -Oral, IV, topical | (N=1805) 20 topical; 21 oral and 2 injectable products | Google search for glutathione distributors | 2 mos. (Feb to May 2008) | NS | NS |

2.Systematic review & KII Electronic databases (Cochrane Library, Medline, HERDIN Online, Western Pacific Region Index Medicus, and

Clinicaltrials. gov)

up to September 2008

| 6. Dofitas 2009 ⁴³ | UP-PGH | Narrative review | Oxidative stress diseases (Chronic skin diseases, skin cancers, allergic and inflammatory skin diseases); Skin whitening | Glutathione -Oral, IV | NA | NA | NA | NS | NS |
|--------------------------------------|--------|--|--|--|--|---|---------|----|------|
| 7. Gicaro 200944 | UP-PGH | RCT | Venous leg ulcers | Natural Philippine honey (Tobee's Apiary) Applied BID x 12 wks. | 18 | OPD | 12 wks. | Y | NS |
| 8. Ledesma 2017 ⁴⁵ | RITM | RCT Cross- sectional (patch test) | Lichen simplex chronicus | Bee propolis 5% ointment (from <i>Apis melifera</i> , Alfonso, Cavite) Applied BID | 80 | Dermatology OPD | 2 wks. | Y | None |
| 9. Ng 2016 ⁴⁶ | SPMC | Critical appraisal of an RCT | Atopic eczema | Human breast milk (hind milk) Applied BID | 1 RCT (N=116) | NS | 2 wks. | NA | None |
| 10. Pardo 2013 ² | UP-PGH | Cross- sectional survey & KII | САМ | Knowledge, attitudes and practices | 114 | PDS dermatologists and trainees | 3 mos. | NS | None |
| 11. Ramos 2007 ⁴⁷ | ОММС | RCT, vehicle- - and active- controlled (3-arm) | Atopic eczema | Topical probiotics (culture of <i>Bacillus, Lactobacillus,</i> <i>Saccharomyces,</i> <i>Anetobacter</i>) Applied BID x 4 wks. | 67 | Dermatology department 2 mos. to 12 yrs. | 4 wks. | NS | NS |
| 12.Sabido 2013 ⁴⁸ | SLMC | Critical appraisal of an RCT | Psoriasis | Weight loss Low calorie diet | 1 RCT (N=61) | Psoriasis OPD, Univ. of Verona, Italy On cyclosporine 2.5 mkd/day | 24 wks. | NA | None |
| 13. Villasenor 2015 ⁴⁹ | SLMC | Critical appraisal of a systematic review/ meta- | Psoriasis | Weight loss (diet, exercise or both) | 1 meta-analysis (N=7 RCTs) Searched up to August 2014 | Obese patients with psoriasis | NS | NA | None |

metaanalysis