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# SYSTEMATIC REVIEW: MECHANISM OF ACTION ORAL AND TOPICAL RETINOL (*Retinyl palmitate*) AS A THERAPY OF ACNE SKIN IN BEAUTY PRODUCTS

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**ABSTRACT**

Acne is one of the dermatological diseases that often appears in adolescence to adulthood. Retinol (*retinyl palmitate*) is a first-generation vitamin A derivative used for acne therapy by reducing sebum production which can cause acne bacteria to grow. This study aims to determine the effectiveness and safety of oral and topical retinol preparations. The method used in the study is systematic review using the PubMed search engine and google scholar according to keywords using the PICO method. Articles that can be downloaded with a period of 2013-2023 for the next article are downloaded in selection according to the criteria, namely inclusion and exclusion. The results of the selection of inclusion criteria there are 12 journals to discuss the effectiveness and safety related to topical preparations and peroral retinol as anti-products acne. The mechanism of action of topical retinol is to reduce the production of micro-comedones caused by the bacteria *Propionibacterium acnes* (*P. acne*) for oral retinol has the mechanism of action works by inhibiting the production of sebum by androgen hormones in the *3-alpha-hydroxysteroid oxidation* pathway using the enzyme *retinol dehydrogenase* to retinaldehyde to be able to dissolve and be delivered at the destination. Oral or topical retinol preparations provide different side effects. Topical retinol has a lower rate of side effects compared to oral retinol. The level of safety and effectiveness of topical retinol preparations is better than oral retinol.

**Keywords:** Per oral and topical retinol; Acne skin; Mechanism of action retinol; *Retinyl palmitate*; Systematic reviews

## 1. INTRODUCTION

*Acne vulgaris* is a skin disease that generally occurs in adolescence and adulthood commonly referred to as acne that appears on facial skin in various parts of the world (Rocha & Bagatin, 2018). Acne can arise caused by internal and external factors, external factors include sun exposure, pollution, and the use of inappropriate types of cosmetics causes the growth of bacteria in the skin (Dréno et al., 2020) accompaniment for internal factors, namely genetic and hormonal (Gollnick, 2015). Vitamin A was used as an anti-acne therapy in the 1940s with oral dosage forms. Tretinoin, which is a derivative of the first generation of vitamin A, has a working action to the number of acnes found on the face, tretinoin preparations in the form of oral tretinoin (Aryal & Upreti, 2017), but the use of oral tretinoin preparations has unexpected side effects, namely keratinization and ichthyosis. Side effects of tretinoin that are not expected to be later developed are topical preparations with active substances as anti-acne is retinol.

Retinol is a derivative of the first generation of vitamin A which has physical chemical properties, namely in the form of a yellow liquid, has low solubility (Bernauer et al., 2016) or is difficult to dissolve in water but can dissolve in organic solvents acetone, chloroform, ethanol, and isopropanol. Retinol palmitate has a mechanism of action that stimulates proliferation in the epidermis layer which is able to regulate sebum production in the skin by converting retinol

through the cleavage of ester bonds into acids retinoate (Zasada & Budzisz, 2019). There are two retinol preparations on the market, namely topical retinol and oral retinol, oral retinol has a working action by increasing oil production (sebum) which has the aim of triggering the occurrence of dead skin cells which can then be replaced with new skin cells (Aryal & Upreti, 2017).

Topical retinol as an anti-acne has a working action capable of carrying out the process of keratinocytes in skin follicles and hyperproduction of sebum in the sebaceous glands to affect the production of bacterial microorganisms *Propionibacterium acnes* (P. acne) which can interfere with drugs to enter through hair follicles in the skin layer (Latter et al., 2019). Oral and topical retinol as preparations used for anti-acne therapy each has side effects (Nast et al., 2016) that are not desired by the patient so that there needs to be control or Evaluation of oral and topical retinol preparations to be able to be safe to use and have a good level of effectiveness.

*Systematic review of* one of the methods used in this study to determine the use of oral and topical retinol preparations that are safe to use. The *systematic review* method uses a *critical appraisal* approach which aims to facilitate the selection of articles that have been downloaded in accordance with inclusion and exclusion criteria. Articles that are included in the inclusion criteria will be reviewed on the theme or title used as this study, namely topical retinol and per processing as therapy anti-acne.

## 2. METHODS

This research was done from September 2021 – January 2022. Research materials collection required five months. The article search engine used in searching for articles is PubMed and *Google scholar* with a period of 2013-2021 using keywords based on PICO. The PICO criteria systematic review of the mechanism of action retinol (*retinyl palmitate*) as beauty product for acne skin can be seen attachment in **Table 1**.

- **P (population/problem)**: The population or problem to be analyzed is in accordance with a predetermined theme.
- **I (intervention)**: An act of management of individual or community cases as well as an explanation of study management in accordance with predetermined theme.
- **C (comparation)**: Intervention or other management used as a comparison, if there is no control group can be used in the selected study.
- **(outcome)**: Result or outcomes obtained in previous studies that are in accordance with predetermined theme.

The research approach to the mechanism of retinol (*retinyl palmitate*) as a cosmetic product for acne skin uses the PICO method to make it easier to search literature as data to ensure the research you are looking for is appropriate. PICO obtained for title, namely the mechanism of action of retinol (*retinyl palmitate*) as a cosmetics product for acne prone skin.

**P**: Acne skin
**I**: Topical and oral retinol preparations
**C**: Other preparation (other than retinol)
**O**: Retinol safety for beauty

Keyword analysis based in PICO and Boolean operators (and, or not or and not) obtained keywords namely oral retinol and topical retinol, the efficacy of retinol tablets and cream, and toxicity oral retinol or retinol cream.

The data collection strategy uses search engines, namely *Google scholar* and PubMed using keyword that have been created with a time span of 2013-2023 for further articles that are in accordance with the title of this retinol research to download the article. Articles that have been downloaded carry out further screening as many as 2000 articles are related to fall into the inclusion and exclusion categories.

**Table 1.** Criteria for The PICO Systematic Review of the Mechanism of Action of Retinol (*retinyl palmitate*) as a beauty product for acne skin.

| PICO Framework | Criteria | |
|---|---|---|
| | **Inclusion** | **Exclusion** |
| P: Population | Studies that focus on the use of retinol for acne prone skin problems. | Studies that review retinol not for acne-prone skin. |
| I: Intervention | Study of the effects of oral and topical retinol preparations. | Studies that do not discuss the effect of oral and topical retinol preparations. |
| C: Comparation | The group of samples that used the retinol for acne in various formulations. | The groups of samples that used combination retinol and other product. |
| O: Outcomes | Effect and mechanism of retinol as a cosmetic product that is safe for use by the public. | Effect and mechanism of retinol as non-cosmetic product. |

The research method of the mechanism of action of retinol as an anti-acne is *a systematic review* with a *critical appraisal* approach. *Critical appraisal* is a method to facilitate the selection of downloaded articles to be examined more deeply according to inclusion and exclusion criteria (Nursalam, 2020). The selection of articles that have been downloaded using several questions that have been made as parameters on the form of *critical appraisal checklist of cross-sectional studies* (Ningtiyas, 2020). Critical appraisal check list cross sectional studies are the stages used in selecting articles that have been downloaded articles, which then scores the articles to make it easier to categorize articles as inclusion or exclusion criteria. Checking articles based on the acquisition score from critical appraisal check list cross-sectional form aim to save time in selecting 54 articles related to retinol as an anti-acne.

Inclusion criteria are criteria that need to be met by each population that can be taken as a sample. The exclusion criteria were that the research subjects could nor-represent the sample because they did not meet the requirement as a research sample. Selection of articles that have been downloaded using several questions that have been made as parameters on the form of critical appraisal checklist of cross-sectional studies (Ningtiyas, 2020) by giving an assessment score to articles that are considered in accordance with the research mechanism of action of retinol as an anti-acne i.e., "yes" has a score of 1 and "unclear", "no", "does not apply " has a score of 0 (Marbawi & Salim, 2019). The flow of selecting downloaded articles on the research mechanism of retinol as an anti-acne can be seen in the prism diagram in attachment **Figure 1**.

## 3. RESULTS AND DISCUSSION

Selection of articles in a systematic review study of the mechanism of action of retinol in acne skin beauty products uses prism diagrams, prism diagrams are used to provide a description of the selection flow of downloaded articles using the article search engine, namely *Google scholar* (identification). Articles are suitable for use as research material, namely screening, suitability, and articles used.

The prism diagram of the study for a systematic review of the mechanism of action of retinol in beauty products for acne-prone skin is to get the results of article screening carried out for 2000 downloaded articles, 54 articles according to parameters, namely abstracts, methods and conclusions in each article that was selected.

Articles that pass the screening stage are generally carried out for suitability or feasibility of an article by making inclusion and exclusion categories based on an assessment score. The scoring score aims to make it easier to categorize articles by inclusion and exclusion. Articles that passed and were included in the inclusion category of 54 articles which had been carried out in several stages of selection resulted in 12 articles entering the inclusion category, of which 12 articles could be used as references. Prism diagram can be seen in attachment **Figure 1**.

Systematic review of the mechanism of action of retinol in this study using two article search engines, namely PubMed and *Google Scholar*. The purpose of using two search engines to facilitate and determine articles that are often published based on a predetermined time span. The

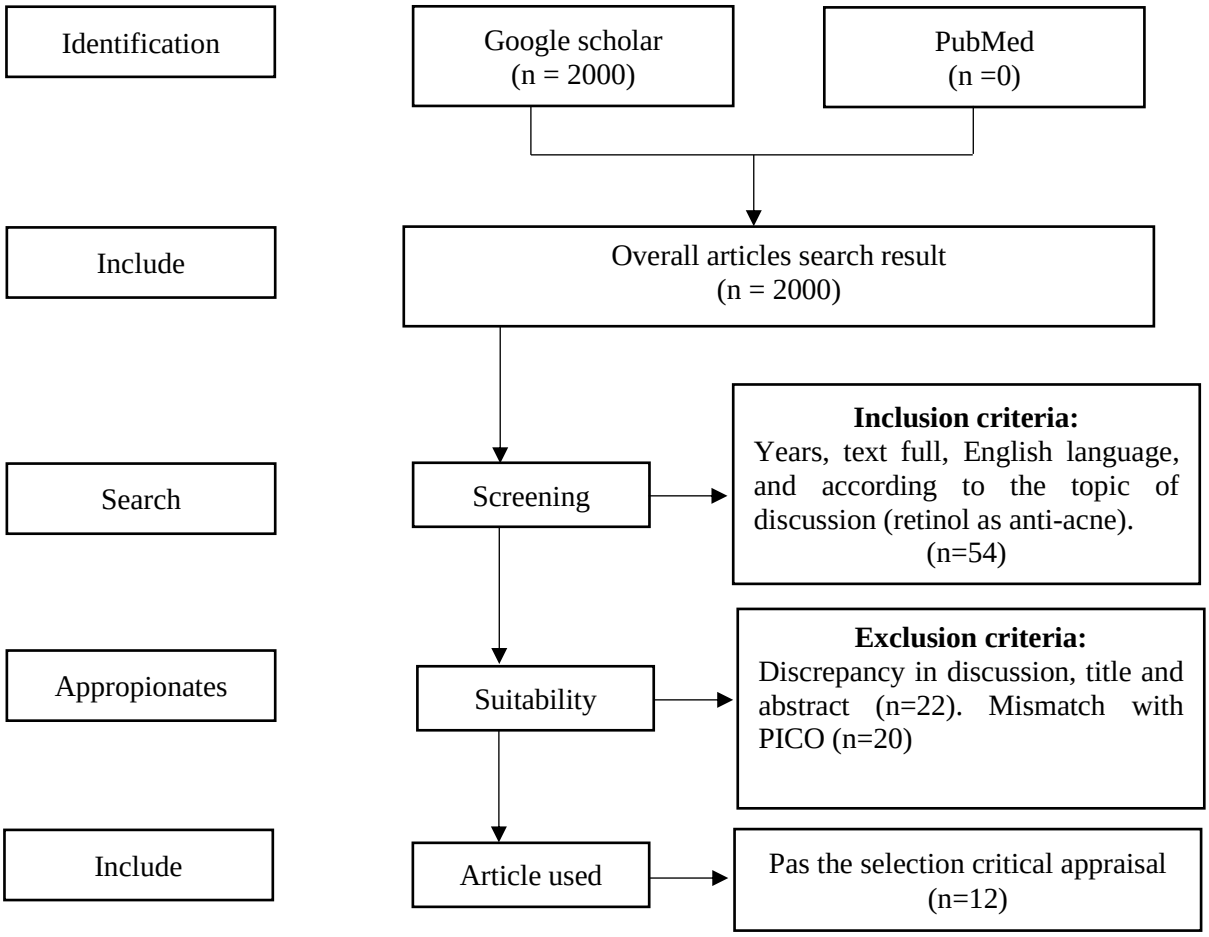


**Figure 1**. Search Result and Article Selection using Prism Diagram Mechanism of Action of Retinol as an Anti-Acne Cometic on the Skin

article the mechanism of retinol as an anti-acne is searched on search engines using keywords based on PICO, PICO is a method of compiling keywords to facilitate search articles and as data to ensure the research articles are sought appropriate.

Article identification was done through a database on search engines using keywords based on PICO according to *keywords* and *Boolean* operators (and, or not or and not) to expand or specific searches in an article (Nursalam, 2020). Keywords obtained to find articles are *retinol cream and retinol tablets, efficacy retinol cream and retinol tablets, and toxicity retinol cream and retinol tablets* on the PubMed article search engine and *Google scholar*. Then articles are downloaded as raw data that needs to do deeper selection or screening using the critical *appraisal* approach method.

The selection of articles from two article searches engines, namely PubMed and Google scholar found for PubMed as many as zero articles and *google scholar* as many as 2000 articles with a period of time articles published at the beginning of the year 2013-2021. Google scholar search engine which has 2000 published articles is downloaded for further selection of articles using the *critical appraisal* method.

The *critical appraisal* approach method is used to make it easier to assess the quality of articles from each study design in an article. Articles that have been downloaded are selected based on questions that have been made on the *critical appraisal check list form of cross-sectional studies* by giving a score of 0-1 (Marbawi & Salim, 2019). (The result of assessment of each article to sort articles into the inclusion and exclusion categories using form critical appraisal check list cross-sectional can be seen in attachment **Table 2**.

**Table 2.** Results of Article Selection by Exclusion and Inclusion.

| No | Title | Year | Score | Criterion | |
|---|---|---|---|---|---|
| | | | | Inclusion | Exclusion |
| 1 | Oral Retinol | 2009 | 5 | √ | |
| 2 | Clinical Evidence on The Efficacy and Tolerability of a Topical Medical device Containing Benzoyl peroxide 4%, Retinol 0.5%, Mandelic Acid 1% and Lacton ionic acid 1% in The Treatment of Mild Facial Acne: An Open Label | 2015 | 4 | | √ |
| 3 | A Brief Review on Systemic Retinoids | 2017 | 8 | √ | |
| 4 | Why Topical Retinoids Are Mainstay of Therapy for Acne | 2017 | 7 | √ | |
| 5 | Development of Cosmeceutical Cream for Dermatitis and Acne Vulgaris Efficacy and Safety of Topical Clascoterone Cream 1% for Treatment in Patient with Facial Acne Two Phase 3 Randomized Clinicals Trial | 2017 | 2 | | √ |
| 6 | Smart lipids As Third Solid Lipid Nanoparticle Generation-Stabilization of Retinol for Dermal Application | 2017 | 1 | | √ |
| 7 | Pilot Study Enhancement of The Antioxidant, Anti-Tyrosinase, and Nti-Hyaluronidase Activity of Morus alba L. Leaf Extract by Pulsed Electric Field Extraction | 2017 | 3 | | √ |
| 8 | A Green Ultrasound-Assisted Extraction Optimization of the Natural Antioxidant and Anti-Aging Flavonolignans from Milk Thistle Silybum marianum (L.) Gaertn. Fruits for Cosmetic Applications | 2017 | 3 | | √ |
| 9 | Molecular Basis of Retinol Anti-Aging Properties in Naturally Aged Human Skin In Vivo | 2017 | 4 | | √ |
| 10 | Dermatology: How to Manage Acne Vulgaris | 2017 | 5 | √ | |
| 11 | Crysin Ameliorates, Malfunction of Retinoid, Visual Cycle Through Blocking Activation of AGE-RAGE-ER, Stress in Glucose-Stimulated Retinal Pigment, Epithelial Cells and Diabetic Eyes | 2018 | 3 | | √ |
| 12 | Targeted topical Delivery of Retinoids in The Management of Acne Vulgaris: Current Formulations and Novel Delivery Systems | 2019 | 7 | √ | |
| 13 | Retinoids: Active Molecules Influencing Skin Structure Formation in Cosmetic and Dermatological Treatments | 2019 | 6 | √ | |
| 14 | Randomized Phase 3 Evaluation of Tarotene 50µg/g Cream Treatment of Moderate Facial and Trunal Acne | 2019 | 3 | | √ |
| 15 | Efficacy and Tolerability of Double-Conjugated Retinoid Cream vs 1.0% Retinol or 0.025% Tretinoin in Subject with Mild to Server Photoaging | 2019 | 2 | | √ |
| 16 | Penetration Smart lipids as Third Solid lipid Nanoparticle Generation-Stabilization of Retinol for Dermal Application | 2019 | 2 | | √ |
| 17 | Review Article: Advances and Challenges in Retinoid Delivery Systems in Regenerative and Therapeutic Medicine | 2020 | 5 | √ | |
| 18 | Nonprescription Acne Vulgaris Treatments: Their Role in Our Treatment Armamentarium-An International Panel Discussion | 2020 | 8 | √ | |
| 19 | The Detrimental Side Effects of Retinol: Beyond Beauty Products | 2020 | 7 | √ | |
| 20 | Collagen Hydrolysates for Skin Protection: Oral Administration and Topical Formulation | 2020 | 3 | | √ |
| 21 | Acne: An Open Label Pilot Study Enhancement of The Antioxidant, Anti-Tyrosinase, and Nti-Hyaluronidase Activity of Morus alba L. Leaf Extract by Pulsed Electric Field Extraction | 2020 | 1 | | √ |
| 22 | Effect of Topicals Application of Nano Retinol on Mild to Moderate Acne Vulgaris | 2022 | 8 | √ | |

The scores obtained for analysis are then included in the criteria for inclusion and exclusion articles. Inclusion criteria are articles that are 50% of good quality and score for exclusion criteria have low quality and score (Nursalam, 2020). The results obtained from the analysis of the *critical appraisal check list of cross-sectional studies* obtained 54 articles in accordance with Retinol's *systematic review* research with the number of included article categories as many as 12 articles and 42 articles entered in the exclusion criteria. The assessment score for inclusion criteria is articles that have a score of 5-8 out of 8 questions and exclusion criteria for articles with a score of 0-4 out of 8 questions. The results of the selection of 54 articles included in the exclusion and inclusion criteria can be seen in **Table 2**.

### 3.1. Topical Retinol

According to El-Samahy et al. (2017) in the article, namely *the effect of topical application of nano retinol on mild to moderate acne vulgaris* stated that topical retinol preparations have a mechanism of action able to reduce the number of acnes on facial skin caused by *Propionibacterium* acne (*P. acne*) bacteria by inhibiting excess oil production (micro blackheads) and able to disguise acne lesions (El-Samahy et al., 2017). Topical retinol in dosage formulations has two methods: conventional and modern. Conventional topical retinol is a drug delivery system with the size of macrolide particles but conventional topical retinol preparations can cause side effects including skin irritation, erythema, and sensitivity to light that causes patients to be non-compliant in completing therapy (Garg, 2016).

Nano lipids are one of the modern approach methods regarding drug delivery systems with reduced particle sizes, nano lipids are expected to provide better effects compared to Conventional topical retinol preparations. The advantage of using a nano lipid delivery system is that it can increase drug permease in the micropore-forming layer located in the stratum corneum (Radtke et al., 2017), reducing the effect inflammation, minimize skin irritation on the face, reduce degradation by UV rays, and reduce the number of acne lesions on facial skin to improve patient compliance (Nadal et al., 2019).

Retinol as an anti-acne therapy is not only in the form of topical preparations but can be prepared orally. Oral retinol dosage formulations that are still in one of the first-generation derivatives of vitamin A, namely isotretinoin. The mechanism of action of isotretinoin orally can reduce sebum production on facial skin, follicular keratinization and intrafollicular concentration (Leung & Barankin, 2015).

Topical retinol has a good level of effectiveness compared to peroral retinol from 34 clinical studies showing a low frequency of irritation. Topical retinol delivery systems are considered better at reducing the number of breakouts and are easier to apply depending on several variables that can affect the effectiveness of retinol as an anti-acne i.e., dose concentration, skin sensitivity and a history of allergy to retinol. Topical retinol provides low side effects. Oral retinol has several side effects that occur, namely interference with the fetus during pregnancy (Aryal & Upreti, 2017) in taking retinol, liver dysfunction (Lee, 2020), and reduce the efficacy of retinol as an anti-acne if consumed together with antibiotics.

### 3.2. Oral Retinol

Oral retinol was able to reduce 90% excess sebum production (Culp et al., 2015) with a duration of consumption of use for 4 weeks to 8 weeks by inhibiting the competitive pathway of *oxidation of 3-alpha-hydrocysteroids* in androgen hormones by *retinol dehydrogenase* enzyme to be able to decrease the production of the hormone's *dihydrotestosterone* and *androstenedione* (Kubba et al., 2009). Retinol soft gel is one of the oral dosage forms taken with two divided doses during fasting and after fasting or after meals at a dose of 0.5-1.0mg/kg body weight. According to (Kubba et al., 2009) in the oral retinol article stated that there were 80 participants for *retinol* per oral dose of 0.5mg/kg body weight for 6 months, the results obtained where 68 participants decreased the number of acnes that grew and 26 participants experienced recurrence due to side

effects of use. Microparticles are a drug delivery system by reducing particle size in expected to reduce the side effects of patient recurrence with a dose of retinol 0.4mg/kg equivalent body weight with a standard dose of 1.0mg/kg body weight.

## 4. CONCLUSION

Retinol is proven to be able to overcome and reduce acne facial skin problems. Topical retinol preparations are considered safer than oral retinol preparations, oral retinol has some unexpected side effects, namely liver dysfunction, causing fetal abnormalities during pregnancy and combined use with antibiotic drugs can reduce the effectiveness of retinol. Side effects of topical retinol are low occurrence of irritation on the face, but it is understandable that the formulation of topical retinol preparations using a nano lipid delivery system has the advantage of the form small particles to be able to deliver retinol into the skin layer so that it can be absorbed directly into the target system.

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## 6. CONFLICT OF INTEREST

All authors declare no conflict of interest.

## 7. REFERENCES

Aryal, A., & Upreti, S. (2017). A brief review on systemic retinoids. *Int J Pharm Sci Res*, *8*(9), 3630–3639. https://doi.org/10.13040/IJPSR.0975-8232.8(9).3630-39

Bernauer, U., Bodin, L., Celleno, L., Chaudhry, Q., Coenraads, P. J., Dusinska, M., Duus-Johansen, J., Ezendam, J., Gaffet, E., & Galli, C. L. (2016). *Scientific Committee on Consumer Safety SCCS OPINION ON Vitamin A (Retinol, Retinyl Acetate, Retinyl Palmitate)*.

Culp, L., Moradi Tuchayi, S., Alinia, H., & Feldman, S. R. (2015). Tolerability of topical retinoids: are there clinically meaningful differences among topical retinoids? *Journal of Cutaneous Medicine and Surgery*, *19*(6), 530–538. https://doi.org/10.1177/1203475415591117

Dréno, B., Shourick, J., Kérob, D., Bouloc, A., & Taieb, C. (2020). The role of exposome in acne: results from an international patient survey. *Journal of the European Academy of Dermatology and Venereology*, *34*(5), 1057–1064. https://doi.org/10.1111/jdv.16119

El-Samahy, M., Sharara, M. A., & Abd Elaziz, S. S. (2017). Effect of topical application of nano retinol on mild to moderate acne vulgaris. *The Egyptian Journal of Hospital Medicine*, *68*(1), 1049–1058. https://doi.org/10.12816/0038208

Garg, T. (2016). Current nanotechnological approaches for an effective delivery of bio-active drug molecules in the treatment of acne. *Artificial Cells, Nanomedicine, and Biotechnology*, *44*(1), 98–105. https://doi.org/10.3109/21691401.2014.916715

Gollnick, H. P. M. (2015). From new findings in acne pathogenesis to new approaches in treatment. *Journal of the European Academy of Dermatology and Venereology*, *29*, 1–7. https://doi.org/10.1111/jdv.13186

Kubba, R., Bajaj, A. K., Thappa, D. M., Sharma, R., Vedamurthy, M., Dhar, S., Criton, S., Fernandez, R., Kanwar, A. J., & Khopkar, U. (2009). Oral retinoids. *Indian Journal of Dermatology, Venereology and Leprology*, *75*, 39.

Latter, G., Grice, J. E., Mohammed, Y., Roberts, M. S., & Benson, H. A. E. (2019). Targeted topical delivery of retinoids in the management of acne vulgaris: current formulations and novel delivery systems. *Pharmaceutics*, *11*(10), 490. https://doi.org/10.3390/pharmaceutics11100490

Lee, M. W. (2020). *The Detrimental Side Effects of Retinol: Beyond Beauty Products*.

Leung, A. K. C., & Barankin, B. (2015). Boxcar acne scars. *Consultant Pediatr*, *14*, 465–474.

Marbawi, M. I., & Salim, T. A. (2019). Mempertahankan keaslian arsip elektronik di era digital berdasarkan tinjauan literatur sistematis. *Berkala Ilmu Perpustakaan Dan Informasi*, *15*(2),

149–162. https://doi.org/10.22146/bip.47370

Nadal, J. M., dos Anjos Camargo, G., Novatski, A., Macenhan, W. R., Dias, D. T., Barboza, F. M., Lyra, A., Roik, J. R., Padilha de Paula, J., & Somer, A. (2019). Adapalene-loaded poly (ε-caprolactone) microparticles: Physicochemical characterization and in vitro penetration by photoacoustic spectroscopy. *Plos One*, *14*(3), e0213625. https://doi.org/10.1371/journal.pone.0213625

Nast, A., Dréno, B., Bettoli, V., Bukvic Mokos, Z., Degitz, K., Dressler, C., Finlay, A. Y., Haedersdal, M., Lambert, J., & Layton, A. (2016). European evidence-based (S3) guideline for the treatment of acne–update 2016–short version. *Journal of the European Academy of Dermatology and Venereology*, *30*(8), 1261–1268. https://doi.org/10.1111/jdv.13776

Ningtiyas, F. W. (2020). *Panduan Literature Review Untuk Skripsi*. Fakultas Kesehatan Masyarakat. Universitas Jember.

Nursalam, H. (2020). Penulisan Literature Review dan Systematic Review Pada Pendidikan Kesehatan (Contoh). *Surabaya: Fakultas Keperawatan Universitas Airlangga*.

Radtke, M., Patzelt, A., Knorr, F., Lademann, J., & Netz, R. R. (2017). Ratchet effect for nanoparticle transport in hair follicles. *European Journal of Pharmaceutics and Biopharmaceutics*, *116*, 125–130. https://doi.org/10.1016/j.ejpb.2016.10.005

Rocha, M. A., & Bagatin, E. (2018). Adult-onset acne: prevalence, impact, and management challenges. *Clinical, Cosmetic and Investigational Dermatology*, *11*, 59–69. https://doi.org/10.2147/CCID.S137794

Zasada, M., & Budzisz, E. (2019). Retinoids: Active molecules influencing skin structure formation in cosmetic and dermatological treatments. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii*, *36*(4), 392–397.