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Hydroquinone in the management of Melasma: therapeutic potential in combined approaches

Hydroquinone in the Management of Melasma: Therapeutic Potential in Combined Approaches

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Summary

This study aimed to investigate, through a systematic literature review, the efficacy of hydroquinone (HQ) as the main depigmenting agent in the treatment of facial melasma, evaluating its clinical effectiveness, tolerability, recurrence rates, and therapeutic potential in combinations. Twenty studies published between 2020 and 2025, selected from PubMed and Google Scholar, in Portuguese and English, were analyzed. The methodology consisted of selecting articles within a specific timeframe and thematic framework, prioritizing randomized clinical trials, systematic reviews, and comparative studies involving HQ alone or in combination with other depigmenting agents or adjuvant technologies. The results demonstrated that hydroquinone, particularly in concentrations of 2% to 4%, remains the gold standard in the treatment of melasma, demonstrating a significant reduction in pigmentation scores (MASI/mMASI) within 60 to 90 days of use. Recent studies support the combined use of HQ with tranexamic acid, tretinoin, lasers, and platelet-rich plasma, achieving faster and more effective results. However, relapses and local adverse effects such as erythema and scaling are still frequent limitations, especially in higher phototypes. The conclusion is that, although new molecules present comparable efficacy, hydroquinone remains the most effective depigmenting agent, especially in combined and supervised regimens, reaffirming its role in evidence-based dermatological practice.

Keywords: Hydroquinone; Melasma; Depigmenting; Combined approaches; Clinical efficacy.

Abstract

This study aimed to investigate, through a systematic literature review, the efficacy of hydroquinone (HQ) as a primary depigmenting agent in the treatment of facial melasma, evaluating its clinical effectiveness, tolerability, recurrence rates, and therapeutic potential in combination therapies.

Twenty studies published between 2020 and 2025 were analyzed, selected from the PubMed and Google Scholar databases, in Portuguese and English. The methodology involved the selection of articles within a defined temporal and thematic scope, prioritizing randomized clinical trials, systematic reviews, and comparative studies addressing HQ alone or in combination with other depigmenting agents or adjuvant technologies. The results indicated that hydroquinone, particularly in concentrations of 2% to 4%, remains the gold standard for melasma treatment, showing a significant reduction in pigmentation scores (MASI/mMASI) within 60 to 90 days of use. Recent studies emphasize the combined use of HQ with tranexamic acid, tretinoin, lasers, and platelet-rich plasma, resulting in greater efficacy and faster clinical response. However, erythema, desquamation, and post-treatment recurrence remain common limitations, especially in higher skin phototypes. It is concluded that, although new molecules and technologies demonstrate comparable efficacy, hydroquinone continues to be the most effective treatment for melasma, particularly when used in combined and supervised regimes, reaffirming its importance in evidence-based dermatological practice.

Keywords: Hydroquinone; Melasma; Depigmenting agent; Combined therapy; Clinical efficacy.

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1. Introduction

Melasma is a chronic and recurrent hyperpigmentation of the skin, of multifactorial origin, which mainly affects photoexposed areas of the face and is prevalent in adult women, especially in tropical countries. It is characterized by increased melanin synthesis and irregular distribution of pigments, impacting not only aesthetics but also well-being psychological health of patients (SARKAR et al., 2023; MAHAJAN, 2022). Melasma can be classified into three main types: epidermal, dermal and mixed, depending on the depth of the melanin deposits. In the epidermal type, there is increased melanocyte activity in the basal layer, leading to superficial and well-defined hyperpigmentation; in the dermis, there is deposition of melanin in the within dermal macrophages; and in the mixed type, both mechanisms coexist. The pathophysiology melasma involves a complex interaction between genetic and hormonal factors, exposure to ultraviolet (UV) radiation and inflammatory processes that stimulate the enzyme tyrosinase in the melanocytes, promoting excessive melanin synthesis (NEAGU, 2022; CHANG, 2023).

For the treatment of melasma, several methods and active ingredients are used that aim to reduce melanin production and even out skin tone. Among the most commonly used are topical depigmenting agents such as hydroquinone, kojic acid, azelaic acid, acid tranexamic acid, cysteamine and thiamidol, in addition to combination therapies with retinoids, corticosteroids and antioxidants. Adjuvant procedures such as peels are also widely used. chemicals, laser therapy, and microneedling. Among these, hydroquinone is the treatment that most presents consistent and lasting results (WATTANAKRAI et al., 2022; FABIAN, 2023).

Hydroquinone has been widely used as a standard therapeutic since the 1990s. 1960, due to its inhibitory action on the enzyme tyrosinase, responsible for the conversion of tyrosine into melanin. However, its side effects such as irritation, erythema and risk of exogenous ochronosis and recurrence after suspension of treatment motivated the search for safer alternatives and therapeutic associations (EL-HUSSEINY, 2020; ARAÚJO; BARBOSA, 2024).

In recent years, clinical studies and systematic reviews have compared the effectiveness of hydroquinone with new depigmenting agents (such as tranexamic acid, thiamidol and cysteamine) and adjuvant technologies (such as laser and microneedling). This combined approach has shown superior results, enhancing efficacy and reducing adverse effects (TEKAM et al., 2022; BARBOSA, 2024; CHANG, 2023).

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2. Methodology

This is a systematic bibliographic review carried out in the PubMed and Google databases Academic, with a time frame from 2020 to 2025. The descriptors used were: hydroquinone, melasma, hyperpigmentation treatment and efficacy, combined by Boolean operators AND/OR.

Clinical articles, systematic reviews and comparative studies on HQ were included. isolated or combined, published in Portuguese and English, focusing on human samples. Duplicate articles, case reports and works without access to the main data were excluded.

The selected articles were organized in a table, containing origin, title, journal, year, language, country and source, as presented in the results section.

Table 1 – Articles used to structure the integrative review.

Origin	Article title	Periodical	Year	Language	Country of study	Source
R. El-Husseiny	*Efficacy and safety of tranexamic acid 5% cream vs hydroquinone 4% in melasma*	J Cosmetic Dermatol (registration node details)	2020	English	Egypt (multicenter study/ registry indicates local population)	https://pubmed.ncbi.nlm.nih.gov/32856757/
N. Neagu	*Melasma treatment: a systematic review*	J Eur Acad Dermatol Venereol (magazine)	2022	English	Review (multiple countries analyzed)	https://pubmed.ncbi.nlm.nih.gov/33849384/
Flavia Kellen Rodrigues Grapevines	Asset Comparison Depigmenting in Relationship to Hydroquinone in the Treatment of Melasma	Aesthetics in Motion Magazine, Vol. 1, No. 2 (2022	2022	Portuguese you	Brazil	https://revista.fumec.br/index.php/esteticaemmovimento/article/view/7993
P. Wattanakrai	Randomized split-face study: topical silymarin vs hydroquinone	J Drugs Dermatol. 21(12):1304–1310	2022	English	Thailand (diverse population in study)	https://pubmed.ncbi.nlm.nih.gov/36468967/
IM Fabian	Topical Hydroquinone for Hyperpigmentation: Narrative review	Dermatol Ther / review (registration)	2023	English	Review (multinational)	https://pubmed.ncbi.nlm.nih.gov/38106810/

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Barbosa, Mayla Martins Conti	Efficacy and safety of 10% nicotinamide combined with 5% magnesium ascorbyl phosphate and 5% hyaluronic acid in cream gel compared to 4% hydroquinone	Double-controlled clinical blind trial the (repository) the Unesp)	2024	Portuguese you		https://repositorio.unesp.br/items/d47dee7d-E6e9-4837-a0ad-fe5492836841/full
R. Sarkar	*Topical and systemic therapy in melasma: system atic review*	*therapie s in melasm the: system attic review* J Drugs Dermat ol / review (registration)	2023	English	Review (multiple countries)	https://pubmed.ncbi.nlm.nih.gov/38099013/
VK Mahajan	Medical therapies for melasma - Revision	Indian J Dermatol Venereol Leprol (registration)	2022	English	Review (India/international) ional)	https://pubmed.ncbi.nlm.nih.gov/35854432/
N. Sadick	*Topical treatment for melasma and post-inflammatory hyperpigmenta tion*	Dermatol Ther (registration)	2023	English	Revision	https://pubmed.ncbi.nlm.nih.gov/37943277/
SS Meymand i	Microneedle dling + topical 4% tranexami c acid vs 4% hydroquin one	J Cosmetic Dermatol / Int J Dermatol (registration)	2020	English	Iran (study registration)	https://pubmed.ncbi.nlm.nih.gov/32406162/
YF Chang	*Efficacy and safety of topical agents in melasm A (network meta-analysis)*	J Eur Acad Dermatol Venereol (registration)	2023	English	Country (multiples review)	https://pubmed.ncbi.nlm.nih.gov/36566490/
PB Lima	*Isobutyl starch thiazolyl resorcinol (Thiami dol) vs 4% hydroq uinone*	J Drugs Dermatol / Int J Dermatol (registration)	2021	English	German there is/study of the multicentric (registration)	https://pubmed.ncbi.nlm.nih.gov/33988887/
Lima, Paula B.	Clinical trials of efficacy in the treatment of facial melasma in women: thiamidol 0.2% and topical cysteamine 5% and picnogen ol 150 mg oral	Doctoral Thesis - University State Paulista (Unesp)	2022	Portuguese you	Brazil	https://repositorio.unesp.br/entities/publication/50e5b218-8789-429d-93ce-85d093bbb c62
H. Wu	*Hexyl sorcinol 1% vs Hydroquinone 2% — Split face RCT*	J Clin Aesthet Dermatol (registration)	2023	English USA	(study population)	https://pubmed.ncbi.nlm.nih.gov/36502500/
J. Nguyen	*Cystea mine cream vs hydroq uinone cream in melasma*	Int J Dermatol	2021	English	USA / multicentric	https://pubmed.ncbi.nlm.nih.gov/32981068/
N. Pazyar	*Intrader mal Tranexa mic Acid vs topical 4% Hydroq uinone*	Dermatol Surg / J Cosmetic Dermatol	2023	English	Iran	https://pubmed.ncbi.nlm.nih.gov/36743976/

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Yara Paloma de Souza Araujo / Isabella of Lima Barbosa	The use of hydroquinone to treat melasma and its relationship with exogenous ochronosis	ochronos and exogenous RECIMA 21 - Magazine Scientific the Multidisciplinary, v.5, n.1, e51513 8	2024	Portuguese you	Brazil	https://recima21.com. br/ index.ph for recima21 /article/vie w/ 5138
S. Mushtaq	*Intralesi onal Tranexa mic acid vs topical 4% hydroq uinone*	Dermatol Surg / J Cosmet Dermatol	2022	English	Pakistan (registration)	https://pubmed.ncbi.nlm.nih.gov/36185872/

Results and discussion

The reviewed studies confirm that hydroquinone remains the depigmenting agent of reference, showing a reduction of up to 60% in pigmentation scores (MASI/mMASI) in 60 to 90 days (EL-HUSSEINY, 2020; WATTANAKRAI et al., 2022).

Combinations with tranexamic acid, tretinoin, and platelet-rich plasma have shown faster results and lower recurrence (TEKAM et al., 2022; BARBOSA, 2024). Trials Brazilians (LIMA, 2022; AMORIM, 2024) reinforce that sequential and combined therapies increase efficacy and improve tolerance.

Recent reviews (NEAGU, 2022; SARKAR, 2023; CHANG, 2023) highlight that, despite of new molecules showing good results, HQ is still the gold standard, especially in Epidermal melasma. However, post-treatment recurrence and adverse effects limit its use. prolonged.

In high phototypes (IV–VI), the risks of irritation and post-inflammatory hyperpigmentation require individualized therapy and rigorous use of photoprotection. HQ continues to be effective and indispensable when used in a supervised manner and in conjunction with other approaches.

Conclusion

The results of this systematic review demonstrate that hydroquinone remains the reference depigmenting agent in the treatment of facial melasma, due to its ability to inhibit tyrosinase and reduce melanin synthesis (FABIAN, 2023; CHANG, 2023). Protocols combined by joining HQ to agents such as tranexamic acid, thiamidol, nicotinamide or technologies

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adjuvants showed greater efficacy and shorter time to clinical response (BARBOSA, 2024; TEKAM et al., 2022).

However, adverse effects and relapses require dermatological monitoring and personalized protocols. The efficacy and safety of HQ depend on the concentration, phototype and time of use (NEAGU, 2022; SARKAR, 2023). It is concluded that, although new molecules show promising results, hydroquinone remains essential in dermatological practice evidence-based, being the most effective and safe treatment when used judiciously and combined.

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