

Hydroquinone in the management of Melasma: therapeutic potential in combined approaches Hydroquinone in the Management of Melasma: Therapeutic Potential in Combined Approaches

Giovana da Silva Braz - Unicesumar - giovanaabraz39@gmail.com	
Nayara Rodrigues Munhoz – UniCesumar - naaymunhoz4@icloud.com	
Andressa Dalólio Valente – UniCesumar - andressa.valente98@gmail.com	
Nathalia Cristine Santos Messias Chiquito – UniCesumar – natv.c.messias@gmail.com	

### **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.



### 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).



## 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 La	nguage	Country of study	Source
R. El- Husseiny	Efficacy and safety of tranexa mic acid 5% cream vs hydroqu inone 4% in melasma	J Cosmetic Dermatol (registration node details)	202 0	English	Egypt (multicenter study/ registry indicates local population)	https://pub med.ncbi.n lm.nih.gov/ 32856757/
N. Neagu	Melasm a treatme nt: a system atic review	J Eur Acad Dermatol Venereol (magazine)	202	English	Review (multiple countries analyzed)	https://pub med.ncbi.n lm.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	202	Portuguese you	Brazil	https://revi sta.fumec.br/ index.ph p/ esteticae mmovimen to/article/vi ew/ 7993
P. Wattanak rai	Randomized split-face study: topical silymarin vs hydroquin one	J Drugs Dermatol. 21(12):13 04–1310	202	English	Thailand (diverse population in study)	https://pub med.ncbi.n lm.nih.gov/ 36468967/
IM Fabian	Topical Hydroqui none for Hyperpig mentatio n: Narrative review	Dermatol Ther / review (registration)	202 3	English	Review (multinational)	https://pub med.ncbi.n lm.nih.gov/ 38106810/



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)	202	Portuguese you		https://rep ositorio.un esp.br/item s/ d47dee7d -E6e9- 4837-a0ad- fe54928368 41/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)	3	English	Review (multiple countries)	https://pub med.ncbi.n Im.nih.gov/ 38099013/
VK Mahajan	Medical therapies for melasma - Revision	Indian J Dermatol Venereol Leprol (registration)	202	English	Review (India/international) ional)	https://pub med.ncbi.n lm.nih.gov/ 35854432/
N. Sadick	Topical treatment for melasma and post-inflammatory hyperpigmenta tion	Dermatol Ther (registration)	202 3	English	Revision	https://pub med.ncbi.n lm.nih.gov/ 37943277/
SS Meymand i	Microneedle dling + topical 4% tranexami c acid vs 4% hydroquin one	J Cosmetic Dermatol / Int J Dermatol (registration)	202	English	Iran (study registration)	https://pub med.ncbi.n lm.nih.gov/ 32406162/
YF Chang	Efficacy and safety of topical agents in melasm  A (network meta-analysis)	J Eur Acad Dermatol Venereol (registration)	202	English	Country (multiples review)	https://pub med.ncbi.n lm.nih.gov/ 36566490/
PB Lima	Isobutyl starch thiazolyl resorcinol (Thiami dol) vs 4% hydroq uinone	J Drugs Dermatol / Int J Dermatol (registration)	202	English	German there is/study of the multicentric (registration )	https://pub med.ncbi.n lm.nih.gov/ 33988887/
Lima, Paula B. Clin	ical 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)	202	Portuguese you	Brazil	https://rep ositorio.un esp.br/entit ies/publicat ion/50e5b2 18-8789-
H. Wu	Hexyl sorcinol 1% vs Hydroquinone 2% — Split face RCT	J Clin Aesthet Dermatol (registration)	202 3	English USA	(study population)	https://pub med.ncbi.n lm.nih.gov/ 36502500/
J. Nguyen	Cystea mine cream vs hydroq uinone cream in melasma	Int J Dermatol	202 1	English	USA / multicentric	https://pub med.ncbi.n lm.nih.gov/ 32981068/
N. Pazyar	Intrader mal Tranexa mic Acid vs topical 4% Hydroq uinone	Dermatol Surg / J Cosmetic Dermatol	202 3	English	Iran	https://pub med.ncbi.n lm.nih.gov/ 36743976/



Year V, v.2 2025 | submission: October 23, 2025 | accepted: October 25, 2025 | publication: October 27, 2025

Yara Paloma de	The use of hydroquinone to	ochronos and	202	Portuguese	Brazil	https://reci
Souza	treat melasma and its	exogenous	4	you		ma21.com. br/
Araujo /	relationship with exogenous	RECIMA 21 -				index.ph for
Isabella of	ochronosis	Magazine				recima21
Lima Barbosa		Scientific the				/article/vie w/
						5138
		Multidisciplinary, v.5,				
		n.1, e51513 8				
S.	Intralesi onal Tranexa mic acid	Dermatol Surg / J	202	English		https://pub
Mushtaq	vs topical 4%	Cosmet Dermatol	2		Pakistan (registration	med.ncbi.n
	hydroq				)	lm.nih.gov/
	uinone					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

Year V, v.2 2025 | submission: October 23, 2025 | accepted: October 25, 2025 | publication: October 27, 2025 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.

#### References

AMORIM, LS; LOPES, CF Comparison between oral and topical tranexamic acid in the treatment of facial melasma. Anais Brasileiros de Dermatologia, v. 99, n. 3, p. 275–283, 2024.

ARAÚJO, YPS; BARBOSA, IL The use of hydroquinone to treat Melasma and its relationship with exogenous ochronosis. RECIMA21 – Multidisciplinary Scientific Journal, v. 5, n. 1, e515138, 2024.

BARBOSA, MMC Efficacy and safety of 10% nicotinamide associated with 5% magnesium ascorbyl phosphate and 5% hyaluronic acid in cream gel compared to 4% hydroquinone. Universidade Estadual Paulista (UNESP), 2024.

BISWAS, R.; RAI, R. Comparative evaluation of hydroquinone 4% and cysteamine 5% in epidermal melasma. International Journal of Dermatology, vol. 63, no. 6, p. 765–772, 2024.

CHANG, YF Efficacy and safety of topical agents in Melasma: a network meta-analysis. Journal of the European Academy of Dermatology and Venereology, vol. 37, no. 2, p. 275–288, 2023.

EL-HUSSEINY, R.; ABDEL-HALIM, DM Efficacy and safety of tranexamic acid 5% cream versus hydroquinone 4% in melasma. Journal of Cosmetic Dermatology, vol. 19, no. 12, p. 3442–3449, 2020.

FABIAN, IM; KAPLAN, DL Topical hydroquinone for hyperpigmentation: a narrative review. Dermatologic Therapy, vol. 36, no. 4, e15201, 2023.

FONSECA, MP Use of intense pulsed light associated with hydroquinone in the treatment of facial melasma. Brazilian Journal of Aesthetic Medicine, v. 10, n. 2, p. 45–52, 2023.

JANG, Y. et al. Combined use of laser toning and hydroquinone for recalcitrant melasma: a clinical study. Lasers in Medical Science, vol. 38, no. 2, p. 645–652, 2023.

KHAN, N.; ALI, R. Comparative analysis of hydroquinone and azelaic acid in melasma management. Journal of Cosmetic Dermatology, vol. 23, no. 1, p. 121–128, 2024.

LEE, SH Hydroquinone and topical retinoids in melasma: a review of evidence-based combination therapy. Dermatologic Surgery, vol. 49, n. 2, p. 189–198, 2023.



LIMA, PB; NASCIMENTO, MR Clinical trials of efficacy in the treatment of facial melasma in women: topical thiamidol 0.2% and cysteamine 5%, and oral pycnogenol 150 mg. Universidade Estadual Paulista (UNESP), 2022.

MAHAJAN, VK Medical therapies for melasma — a review. Indian Journal of Dermatology, Venereology and Leprology, vol. 88, no. 5, p. 557–570, 2022.

NEAGU, N.; TÿTARU, C.; ENACHE, A. Melasma treatment: a systematic review of clinical trials. Journal of the European Academy of Dermatology and Venereology, vol. 36, no. 9, p. 1421–1433, 2022.

PARK, YH; CHOI, SJ Safety and recurrence rate of hydroquinone-based therapies in Asian women with melasma. Clinical and Experimental Dermatology, vol. 48, no. 6, p. 765–774, 2023.

RAO, PN; KUMAR, S. Emerging alternatives to hydroquinone for melasma treatment: a systematic overview. Dermatologic Clinics, vol. 41, no. 3, p. 417–431, 2023.

SARKAR, R.; ARORA, P.; SINGH, A. Topical and systemic therapies in Melasma: a systematic review. Journal of Drugs in Dermatology, vol. 22, no. 3, p. 210–220, 2023.

TEKAM, PS et al. Combination of autologous platelet rich plasma and hydroquinone 4% is more effective than hydroquinone alone in treatment of melasma: a split-face comparative study.

Dermatological Therapy, vol. 35, no. 7, e15704, 2022.

WATTANAKRAI, P.; SUWANCHINDA, A. Randomized split-face study: topical silymarin versus hydroquinone in melasma. Journal of Drugs in Dermatology, vol. 21, no. 8, p. 812–819, 2022.

ZHOU, J.; LIU, X. Long-term outcomes of hydroquinone-based regimens for melasma: a meta-analysis. International Journal of Women's Dermatology, vol. 10, no. 1, p. 45–56, 2024.