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Original Research Article

Expert perspectives on the role of kojic acid in the treatment of hyperpigmentation in dermatology practice in Indian settings

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ABSTRACT

Background: Despite several clinical studies regarding the effectiveness of kojic acid, there is a dearth of studies among clinicians. So, this study aims to gather expert opinions regarding the physician's perspective and preference on the role of kojic acid and its combination in treating hyperpigmentation in Indian settings.
Methods: This cross-sectional study utilized a multiple-response questionnaire of 24 questions designed to gather feedback, clinical observations and specialists' experiences in managing hyperpigmentation with kojic acid and its combinations in routine practice. The questionnaire was structured to capture expert opinion on the frequency of use, perceived efficacy, adverse effects and preferences for these combinations.
Results: The survey involved 375 clinicians, with the majority (45.87%) preferring kojic acid combinations for treating various indications, including melasma, hyperpigmentation and PIH. Approximately 44% of the respondents reported prescribing kojic acid with glycolic acid to 11-20% of their patients. For peri-orbital melanosis, half of the respondents (50.4%) recommended kojic acid as monotherapy for fewer than 10% of patients, while 39% suggested it for 11-20% of patients. Around 77% of clinicians preferred the combination of kojic acid and glycolic acid for melasma treatment and 68.27% occasionally recommended hydroquinone with kojic acid for melasma. The preferred formulation of kojic acid was a gel, chosen by 48.8% of clinicians, while 43% preferred a cream formulation.
Conclusions: This study highlights clinicians' preference for kojic acid combinations, especially with glycolic acid, for treating hyperpigmentation, particularly melasma. Most clinicians prefer gel formulation. These findings emphasize the popularity of kojic acid, especially in combination therapies, for managing hyperpigmentation.

Keywords: Glycolic acid, Hyperpigmentation, Kojic acid, Melasma

INTRODUCTION

The global burden of melasma and post-inflammatory hyperpigmentation (PIH) is significant due to their prevalence, impact on quality of life and associated healthcare utilization. Among the top 11 skin conditions treated by dermatologists, skin pigmentation disorders account for approximately 24.7 million visits annually. In the United States, melasma affects approximately 5 million individuals, with prevalence rates reaching up to 40% in certain populations.[1,2] Globally, melasma is the most common pigmentation disorder, affecting 33.6% of individuals, followed by PIH at 12.5% and freckles at 6.9%.[3,4] Hyperpigmentation disorders are prevalent in countries like India due to a combination of high sun exposure and diverse ethnic backgrounds that influence skin type and susceptibility.[5,6]

A study by Hourblin et al, has reported that 80% of Indian women aged 30 and above experience some form of hyperpigmentation, which contributes to a reduced quality of life due to both aesthetic and emotional

factors.[7] This highlights the need for targeted therapeutic approaches along with preventative measures like photoprotection, which is fundamental for managing these conditions. However, achieving effective depigmentation often requires specific therapeutic interventions tailored to individual needs.[5]

Among various treatment options, kojic acid has gained recognition as a promising depigmentation agent.[5,8,9] It is a naturally derived compound produced by fungi and acts as a potent inhibitor of tyrosinase, an enzyme critical for melanin synthesis. By targeting tyrosinase, particularly its catecholase activity, kojic acid effectively reduces melanin production.[10,11] It is regarded as one of the most effective skin-lightening agents in the beauty industry due to its ability to inhibit tyrosinase.

In addition to its depigmenting properties, kojic acid also exhibits anti-inflammatory and antioxidant effects, further enhancing its therapeutic potential.[10,12,13] The cosmeceutical ingredient review (CIR) has determined that kojic acid is safe for use in cosmeceutical products at a concentration of 1%. Moreover, existing dermatological safety data indicate that kojic acid is also safe at a concentration of 2%, suggesting that an upper limit of 2% may be appropriate for skin treatments.[14]

In vitro studies suggest that combining kojic acid with other skin-lightening agents may enhance its efficacy, demonstrating potential synergistic effects in managing pigmentation disorders.[15,16] The challenge of effectively treating hyperpigmentation remains unresolved, highlighting the potential of kojic acid and its combinations while underscoring the need for innovative treatment options.[17] The present survey is intended to gather clinicians' perspectives on the use of kojic acid and its combinations for managing hyperpigmentation in Indian settings.

METHODS

A cross-sectional multiple-response questionnaire-based study was carried out from June 2023 to December 2023 and included clinicians with experience treating dermatologic diseases.

Questionnaire

The questionnaire booklet titled KITE (Role of Kojic acid in the treatment of Hyperpigmentation) study was sent to the dermatologists who were interested to participate. The KITE study questionnaire consisted of 24 questions, gathering feedback, clinical observations and experiences from specialists regarding the role of kojic acid in managing hyperpigmentation in routine settings.

The study was conducted after getting approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian regulatory authority, drug controller general of India.

Participants

An invitation was sent to leading dermatologists in managing dermatologic diseases in the month of March 2023 for participation in this Indian survey. About 375 dermatologists from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Those who did not provide consent were excluded. Dermatologists were requested to complete the questionnaire without discussing it with peers. Before the initiation of the study, written informed consent was obtained from all the study participants.

Statistical methods

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear insight into their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, graphs and pie charts were created using Microsoft Excel 2019 (version 16.0.17928.20114).

RESULTS

The study included 375 clinicians, of whom approximately 48% reported that 11 to 20% of the population suffers from hyperpigmentation after the age of 45 years. The majority (45.87%) of the clinicians preferred Kojic acid combinations for treating all indications, including melasma, hyperpigmentation and PIH (Figure 1). According to 44% of the respondents, about 11 to 20% of patients were prescribed kojic acid in combination with glycolic acid (Figure 2). More than half (58.4%) of the clinicians stated kojic acid with glycolic acid as the preferred combination (Table 1). Around 62% recommended using the kojic acid combination in patients with hyperpigmentation for 6 to 8 weeks.

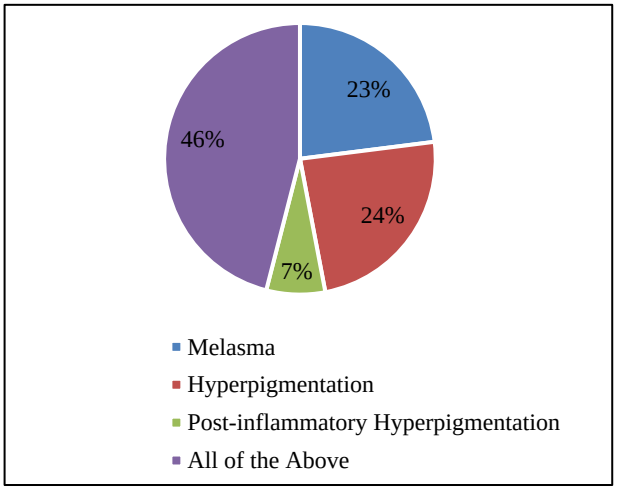

Figure 1: Distribution of response to the preferred indications for kojic acid combination.

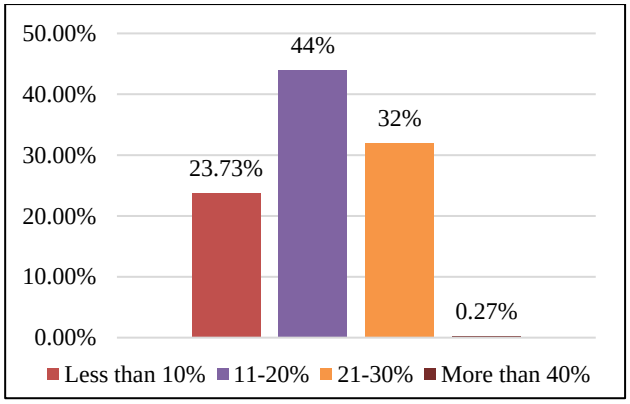

Figure 2: Distribution of response to the proportion of patients prescribed kojic acid in combination with glycolic acid.

Table 1: Distribution of response to the preferred combination of kojic acid.

Preferred kojic acid combination	Response rate (n=375)
Kojic acid with glycolic acid	58.4%
Kojic acid with niacinamide	16.8%
Kojic acid with liquorice extract	24.27%
Kojic acid, glycolic acid and niacinamide	0.27%
Kojic acid with all the above	0.27%

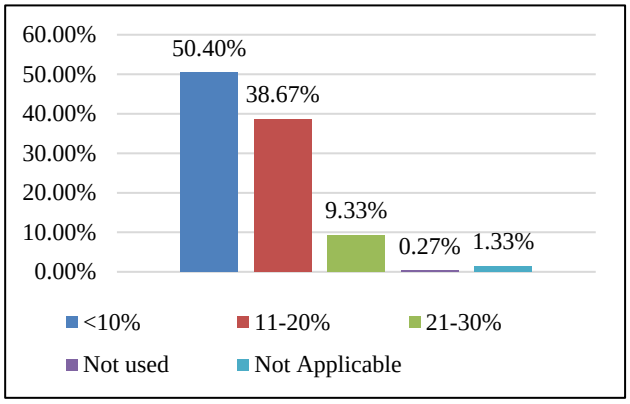

Figure 3: Distribution of response to the frequency of kojic acid recommendation as monotherapy for periorbital melanosis.

The majority (80.8%) of the clinicians advocated the use of sunscreen in treating hyperpigmentation. Half of the respondents (50.4%) recommended kojic acid as monotherapy in peri-orbital melanosis for less than 10% of their patients, while 39% indicated they recommended it for 11 to 20% of patients (Figure 3). Around 77% of the participants preferred a combination of kojic acid and glycolic acid as a demelanizing agent in melasma (Table 2). About 60% of the clinicians recommended a duration of 6 to 8 weeks for the use of kojic acid in perioral melanosis. The majority of the participants (70.4%) opined adding tetrahydro curcumin for treating melasma.

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Table 2: Distribution of response to the preferred demelanizing agent in melasma.

Agents	Response rate (n=375)
Hydroquinone	0.27%
Kojic acid	13.33%
Glycolic acid	7.73%
Combination of kojic acid and glycolic acid	77.33%
Triple combination	0.53%
Silymarin	0.27%
Cysteamine	0.27%
None of these	0.27%

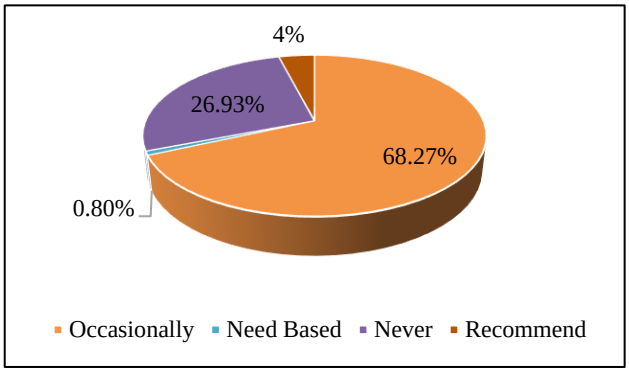

Figure 4: Distribution of response to the recommendations for the use of hydroquinone with kojic acid for melasma treatment.

According to 49% of the clinicians, approximately 11-20% of the population preferred licorice extract for managing hyperpigmentation, while 37% of clinicians recommended it for less than 10% of patients. About 44% of clinicians occasionally preferred hydroquinone combinations as the initial therapy for treating hyperpigmentation. As reported by 48% of the respondents, 11 to 20% of the population were recommended to receive kojic acid for drug-induced hyperpigmentation. Around 55% of clinicians occasionally recommended kojic acid for pigmentation associated with acne. According to 49% of the clinicians, gel is the most preferred formulation for kojic acid, while 43% of clinicians preferred a cream formulation (Table

3). Approximately 62% of clinicians stated they co-prescribe oral tranexamic acid in the management of melasma.

Table 3: Distribution of response to the preferred kojic acid formulations.

Formulations	Response rate (n=375)
Cream	42.93%
Gel	48.8%
Lotion	1.33%
All of the above	6.93%

More than half of clinicians (55.73%) recommended kojic acid combination therapy for 5 to 10% of the teenage population, while 35% recommended it for less than 5%. Around 68% of the participants preferred an oral antioxidant in the treatment of melasma and hyperpigmentation. About 55% of clinicians occasionally recommended kojic acid for treating freckles, while 39% do not use it. The majority of clinicians (44.27%) preferred individual one-to-one sessions for patient education, while 34% opined using social media, radio, television or print media for educating patients.

DISCUSSION

The present survey emphasizes the preference for kojic acid and its combination in treating hyperpigmentation. In the survey, most of the clinicians preferred kojic acid combinations for treating melasma, hyperpigmentation and PIH. In line with these findings, Nayak et al, corroborated the depigmenting effect of kojic acid singly or in combination.[18] Deo et al, in a comparative study concluded kojic acid combination showed a 60% improvement in melasma area severity index (MASI) scores to monotherapy.[19] Wawrzyk-Bochenek et al, using a hyperspectral camera demonstrated that kojic acid significantly reduces skin discoloration.

In 75% of patients tested, it increased skin brightness, reduced skin contrast by approximately 83% and improved skin homogeneity by 67%.[10] A survey involving 235 dermatologists from India revealed that 58% preferred kojic acid-based combinations for treating hyperpigmentation, while 47.45% strongly agreed that kojic acid-based formulations could serve as a safe alternative to steroid- and hydroquinone-based formulations. The findings concluded that novel kojic acid-based formulations may be an effective therapeutic option for managing epidermal hyperpigmentation.[4]

The present study also highlighted that kojic acid combined with glycolic acid is the most frequently prescribed demelanizing agent. Supporting these findings, Garcia and Fulton concluded that kojic acid in combination with glycolic acid was highly effective in reducing the pigment in melasma patients.[20] Pérez-Bernal et al, observed that kojic acid, either as a standalone treatment or in combination with glycolic acid or hydroquinone, has demonstrated favorable results in managing hyperpigmentation, primarily due to its tyrosinase-inhibiting properties.[21] Furthermore, a split-face study comparing a 2% kojic acid and 5% glycolic acid formulation with 2% hydroquinone and 5% glycolic acid found both combinations to be equally effective in treating melasma.[22]

Majority of the current survey respondents recommended kojic acid as monotherapy for peri-orbital melanosis patients. A comprehensive review by Sarkar et al, highlighted kojic acid as one of the available alternatives for managing peri-orbital hyperpigmentation.[23]

The present survey highlighted the occasional use of hydroquinone combined with kojic acid for treating melasma. Supporting this, a study involving 39 patients demonstrated that combining hydroquinone with kojic acid or glycolic acid significantly reduced the severity of melasma.[4] The inclusion of 2% hydroquinone in kojic acid-based formulations further enhanced their overall efficacy. This synergy arises from their complementary mechanisms, as hydroquinone and kojic acid target different stages of melanogenesis, leading to superior therapeutic outcomes compared to monotherapy.[24,25] Additionally, a 12 weeks study evaluating a formulation comprising hydroquinone (2%), kojic acid (1%) and glycolic acid (2%) reported a 24.2% reduction in the melasma area severity index (MASI). The findings suggest that such combinations are effective in reducing pigmentation and achieving mild improvements with good tolerability.[26]

The majority of the present survey respondents preferred gel-based formulations of kojic acid. These formulations, particularly those developed using microemulsions or systems based on carbomer, offer improved solubility and bioavailability, addressing common challenges associated with kojic acid. Such advancements enhance skin penetration and ensure efficient delivery while minimizing irritation risks. Microemulsion-based gels, in particular, provide sustained drug release and improved photostability, making them ideal for daytime applications. These formulations minimize degradation from sunlight, ensuring prolonged efficacy and stability.[27,28]

The current study findings can support clinicians in making informed decisions and improving patient care by incorporating insights into the preferences and prescribing practices of kojic acid and its combinations for treating hyperpigmentation in Indian settings. Major strengths of the survey include its large sample size and the use of a well-designed, validated questionnaire for data collection from clinicians. However, some limitations warrant consideration. The results may be influenced by potential bias due to reliance on expert opinion, with varying perspectives and preferences among clinicians affecting the outcomes. Moreover, the survey may not fully capture emerging evidence or

evolving trends in hyperpigmentation management. A key limitation is the lack of extensive literature specifically addressing the use of kojic acid and its combinations in hyperpigmentation treatment, which hinders a broader understanding of its effectiveness. These limitations should be considered when interpreting the results. To overcome these challenges, future prospective trials or real-world observational studies are recommended to validate the survey findings and offer a more comprehensive understanding of optimal treatment strategies for hyperpigmentation.

CONCLUSION

The survey highlights clinicians' predominant preference for kojic acid combinations, particularly with glycolic acid, for managing hyperpigmentation, including melasma and peri-orbital melanosis. Among demelanizing agents, the kojic acid and glycolic acid combinations are most frequently utilized, especially for melasma treatment. Gel formulations of kojic acid are preferred by nearly half of the clinicians, with creams being the second choice. These findings underscore the widespread adoption of kojic acid, especially in combination therapies, as a standard approach for managing hyperpigmentation in clinical practice.

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