Topical melatonin, resveratrol, and rapamycin for skin anti-aging: a systematic review

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BACKGROUND

● With an abundance of skincare products available today claiming to slow or reverse signs of aging, patients may feel overwhelmed selecting products.

● Topical melatonin, resveratrol, and rapamycin have recently emerged as potential off-label treatments for skin aging.

OBJECTIVE

The purpose of this systematic review was to perform a comprehensive review of the literature on these three agents when used for the reduction of the symptoms of aged skin, and their corresponding effectiveness, or lack thereof.

METHODS

● Search Strategy & Study Selection

A comprehensive search strategy using a combination of controlled vocabulary and keywords for “topical melatonin”, “resveratrol”, “rapamycin”, and “skin aging” was developed with the expertise of an experienced health sciences librarian.

● Articles were identified through a systematic search of the following bibliographic databases: PubMed/Medline (NLM), Embase (Elsevier), Cochrane Library (Wiley), International Pharmaceutical Abstracts (Ovid), Web of Science (Clarivate Analytics), and Scopus (Elsevier), along with citation searches of key articles, and grey literature.

● Three investigators individually assessed each of the studies based on the study design, intervention, participants, outcomes, and results, determining eligibility for inclusion.

● Human studies published up to September 2019 were included if at least one group received topical melatonin, resveratrol, or rapamycin, and at least two outcomes related to skin anti-aging were reported.

● Disagreements on inclusion were resolved through consensus generation with an additional reviewer, and bias assessment was performed.

Risk of Bias Assessment

Bias was assessed using one of two tools, depending on study type: internal and external validity. Risk of Bias Assessment

Table 1: Data Extraction Table

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Duration</th>
<th>Design</th>
<th>Subject Baseline Characteristics</th>
<th>Outcome Results</th>
</tr>
</thead>
</table>
| Topical Melatonin
| Sagen (2017) | Topical melatonin 1% gel | Restricturn 5 mL, topically daily | 4 weeks | RCT | Not mentioned | + Increase in sebum + No change in skin pigmentation |
| Morgan (2012) | Topical melatonin + other BID | Carrier + supplement BID | 8 weeks | RCT | Dry skin with moderate vescication and pigmentation | In subjects that received supplement and topical product – Lipids increased from about 40 to 70% + Hydration increased from 55% to 100% |
| Puviran (2019) | Topical melatonin + 2% retinyl palmitate BID | No treatment | 2 months | Split-face | Moderate-severe facial aging | + Decreased carotenoid volume (+3%) + Decreased wrinkles (+19%) + Decreased melanin content (+7) | + Reduced porosity volume (+11%) |
| Mani (2018) | Topical melatonin 2% gel | No treatment | 3 months | Pre-post | Moderate-severe skin aging | + Reduction in crow’s feet (+10%) + Surface microfolds (+25%) + Reduction in skin roughness (+7%) in wrinkles + Reduction in skin roughness (+4%) and skin pores (+6%) + Reduction in facial pores and UV spots + No changes in skin tone + Reduction in skin roughness (+4%) + Reduction in 2% reduction of the total wrinkle | + Improvement in skin firmness and quality + Improvement in skin tone evenness + Improvement in skin quality + Improvement in skin roughness + Improvement in skin texture + Improvement in skin radiance |
| Gottlieb (2019) | Topical melatonin + other BID | No treatment | 3 months | Pre-post | Pre-post assessment | + Moderate-facial aging with crow’s feet wrinkles and 2% pigtomitted | + Reduction in wrinkles (+11%) + Increase in skin firmness (+38%) + Reduction in redness (+70%) + Overall improvement in skin quality and complexion |

RESULTS

● The majority of selected studies were pre-post design and enrolled female patients aged 40-65 years.

● 11 studies included the agents of interest as components of a combination regimen.

● In the 5 studies involving topical melatonin, positive outcomes included skin wrinkled reduction, improved skin hydration, and improved skin texture or complexion.

● In the 11 studies involving resveratrol, positive outcomes included reduction in skin wrinkles, hyperpigmentation, or age spots, and improvement in skin elasticity and tonicity or complexion.

● Only one article on rapamycin met inclusion criteria and the positive outcomes of this study included an increase in dermal thickness, diameter, and density of collagen fibers.

DISCUSSION & CONCLUSIONS

Available studies identified through this systematic review suggest that resveratrol and topical melatonin appear to be modestly effective at reducing the appearance of aged skin.

While both of literature exists that addresses rapamycin suggest that resverapycin can be a therapeutic option for the treatment of skin aging, additional studies are required to confirm these findings.

REFERENCES

● All authors of this presentation have nothing to disclose regarding personal financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.