WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 7, 32-37. Review Article ISSN 2277– 7105

THE USE OF ANACARDIACEAE FAMILY'S VEGETABLE EXTRACTS AS NATURAL SKIN-CLEARING AGENTS: A REVIEW

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Article Received on
24 April 2020,

Revised on 14 May 2020,
Accepted on 04 June 2020

DOI: 10.20959/wjpr20207-17131

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ABSTRACT

Anacardiaceae is a family of great economic importance, has approximately 81 genres and 800 species. The aim of this paper is to relate the species of the Anacardiaceae family that have tyrosinase inhibitory activity, or other mechanism of action of bleaching, either in vitro or in vivo experimental models. This systematic review was carried out through a literature search performed in 2014 to 2019. This literature search was performed through specialized search databases, using several combinations of the following keywords: “Anacardiaceae and skin whitening”; “Anacardiaceae and tyrosinase”; “Anacardiaceae and hypermellosis”. 49 articles were identified. Out of this total, 4 articles were selected as the others did not meet the inclusion criteria. In these articles we researched the plant species, part of the plant used, methodologies used, and results obtained. The results show that species of the Anacardiaceae family have high market potential and may emerge as a differentiated vegetable raw material and that a continuous effort of researchers and cosmetic industries is necessary to expand the studies of these species as skin whitening agents.

KEYWORDS: Anacardiaceae; tyrosinase; hyperpigmentation.

INTRODUCTION

Recent changes in the cosmetic consumer markets' profile combined with the exceptional strength of Brazilian biodiversity have lead to significant innovations in the development of new skin care products (Stallings & Lupo, 2009).

Anacardiaceae is a family of plants that includes numerous species of great economic importance, such as mango, cashew, pistachio and pink pepper. Most are trees or shrubs and are rich in polyphenols, located mainly in tropical areas, but also in subtropical and temperate areas. More recent data report the existence of approximately 81 genres and 800 species (Schulze-Kaysers et al., 2015).

The uniformity of skin color, whether on the face, neck and upper limbs is considered a very important aesthetic attribute in western and eastern cultures. Hyperchromies are pigmentation disorders that originate from overproduction of melanin. These spots may arise due to factors such as aging, hormonal changes, inflammation, allergies and sun exposure, and others (Draelos, 2009; Gonchoroski, Côrrea, 2005).

Bleaching agents can act by different mechanisms of action, but all linked to the production or transfer of pigments, ie: selective destruction of melanocytes; inhibition of melanosome formation and alteration of its structure; inhibition of tyrosinase biosynthesis; inhibition of melanin formation; interference with the transport of melanin granules; chemical alteration of melanin; melanosome and keratinocyte degradation (Draelos, 2009).

Tyrosinase inhibitors are considered important bleaching agents and are used as one of the standard treatments for diseases related to hyperpigmentation. There are several reports in the literature showing a variety of agents from natural sources that act as a competitive inhibitor in tyrosinase monophenolase and diphenolase activities, motivating the prospecting for new natural actives in Brazilian biodiversity (Kim, Uyama, 2005; Jennifer et al., 2012)

Therefore, the aim of this paper is to relate the species of the Anacardiaceae family that have tyrosinase inhibitory activity, or other mechanism of action of bleaching, either in vitro or in vivo experimental models.

METHODOLOGY

This systematic review was carried out through a literature search performed in May 2014 to May 2019. This literature search was performed through specialized search databases: Biblioteca Virtual em Saude BVS (Bireme), PubMed Medline, SciELO and Science Direct, using several combinations of the following keywords: “Anacardiaceae and clareamento da pele”, “Anacardiaceae and tirosinase”, “Anacardiaceae and hipermelose”. The manuscript selection was based on the inclusion criteria: articles published in English and Portuguese and

articles with keywords in the title, abstract or full-text. 49 articles were identified. Out of this total, 4 articles were selected as the others did not meet the inclusion criteria. For the selection of the manuscripts, three investigators first selected the articles according to title, then to abstract and then through an analysis of the full-text publication. Any disagreement was resolved through a consensus between the investigators. The resulting articles were manually reviewed with the goal of identifying and excluding the studies that did not fit the criteria described above.

RESULTS AND DISCUSSION

We identified 49 records (Table 1) indexed in the databases used, with Pubmed showing 10, Scielo with 01, Virtual Health Library with 5 and Science Direct with 33 records. Of this total, 45 manuscripts were excluded from the evaluation because they did not meet the inclusion criteria, because they were repeated in the databases or in more than one descriptor.

Table 1: Number of records in databases.

Databases	Keywords			No. of excluded papers	Consulted Period
	Anacardiaceae e clareamento da pele Anacardiaceae and whitening skin	Anacardiaceae e tirosinase Anacardiaceae and tyrosinase	Anacardiaceae e hipermelanose Anacardiaceae and hypermelanosis		
Pubmed	0	9	1	45	2014 to 2019
Scielo	0	1	0		
Bvs	1	3	1		
Science direct	7	26	0		
Total	49				

When searching the scientific literature, only 04 (four) studies met the adopted criteria (Table 2), being the species searched: Semecarpus caudata, Swintonia floribunda, Pistacia vera and Myracrodruon urundeuva.

In all studies tyrosinase inhibitory activity was demonstrated by in vitro methodology using spectrophotometric method and kojic acid as standard. In the study by Sarkhail et al (2017), in addition to this spectrophotometric methodology, the melanin quantification assay was performed in human melanoma cells.

Phu H. Dang et al. (2018) isolated 06 (six) compounds from Semecarpus caudata stem methanolic extract, being: somecarpon (1), naringerin (2), eriodictyol (3), taxifolin (4), resokaempferol (5) and quercetin (6). The tyrosinase inhibitory activity of all these

compounds was evaluated, and 4, 5 and 6 showed satisfactory activity with IC 50 respectively 6.3; 20.6; 4.5 μg mL^{-1}. The IC 50 of kojic acid was 6.3 μg mL^{-1}, thus, it is clear that taxifolin had the same potency as the positive control and quercetin was higher. As observed, the high concentration of hydroxyls presents in the compounds increased the activity, as can be seen in figure 1.

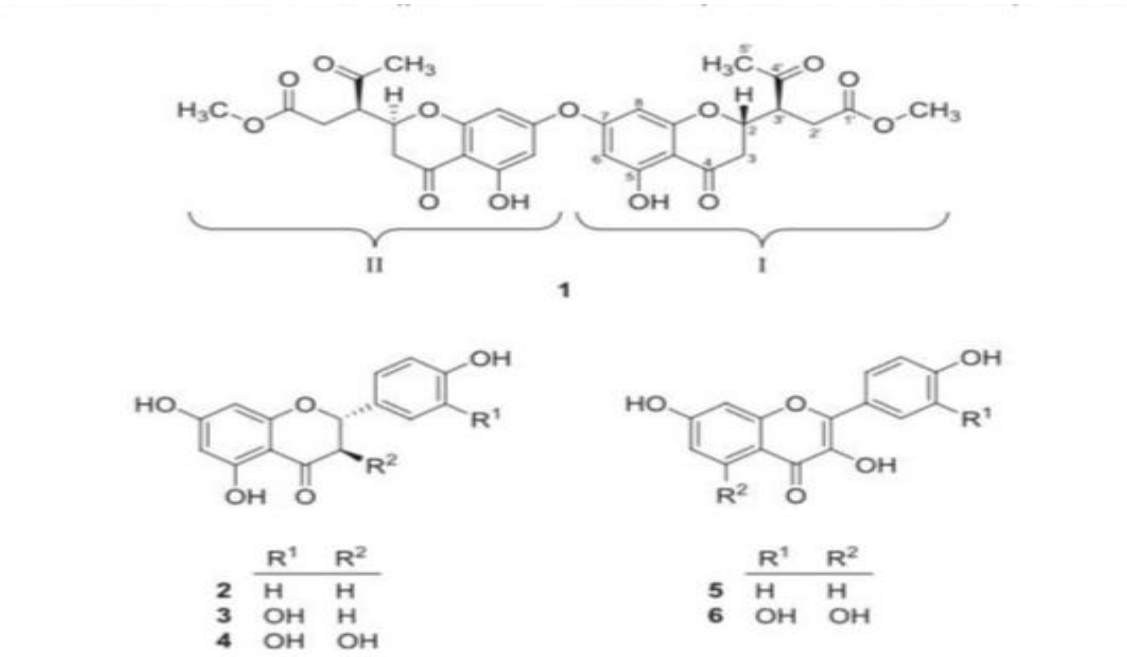

Figure No. 1: Structure of Compounds 1-6 Isolated from Semecarpus caudata (Phu H. Dang et al., 2018).

Phu H. Dang et al. (2018) also conducted another study with Swintonia floribunda species, this time isolating 05 (five) compounds from methanolic extract of stem bark: (1) integracin E, n-heptacosyl trans-ferulate (2), pinoresinol (3), epi-pinoresinol (4) and syringaresinol (5). Integracin E had presented a strong inhibitory effect (IC50, 48.2 μM), which is comparable to that of kojic acid (IC50, 44.6 μM). This activity is due to the hydrophilic resorcinol moiety, which is one of the most popular chemical functional groups that interacts with copper (Cu^{2+}) ions at the tyrosinase active site, whereas the hydrophobic alkyl chain interacts with the hydrophobic moiety near the active site. tyrosinase. Thus, this was the first report on the tyrosinase inhibitory activity of a dimeric alkylresorcinol. The other compounds 2-5 were inactive because they had IC50 values> 100 μM (Phu H. Dang et al., 2018).

Regarding the study involving the species Pistacia vera, the antimelanogenic activity of the methanolic extract of the fruit peel (MPH) was evaluated by the melanin content assay. This extract inhibited melanin synthesis in a dose-dependent manner (IC50 = 0.41 mg / mL). MPH

and kojic acid showed similar inhibitory effect of melanin at a dose of 0.1 mg / mL. For the tyrosinase inhibitory activity, MPH and kojic acid presented IC50 = 0.72 and 0.05 mg / mL, respectively. Thus, it can be seen that MPH activity was not significant for enzyme inhibition (Sarkhail, 2017).

To determine inhibition of tyrosinase enzyme by Myracrodruon urundeuva, hexanic extracts of the leaves and bark of the stem were prepared. In addition, the plant residue was extracted with methanol, providing extracts of M. urundeuva methanolic from the leaves and bark of the stem. At the concentration of 1000 $\mu g.mL^{-1}$, the methanolic extracts showed satisfactory results, showing tyrosinase inhibition percentages of 66% for leaf extract and 42% for stem bark extract. Already the hexane extracts, besides not showing inhibition contributed to the increase of tyrosinase action, with values of 330% for leaves and 109% for the stem. This is possibly due to the fact that they provide phenolic substances capable of acting as a substrate for the tyrosinase enzyme. At the same concentration used for the extract, the positive control, which is kojic acid completely inhibited the enzyme (Vieira *et al*., 2015).

CONCLUSION

In vitro and in vivo studies of plant active applications as bleaching agents are growing and expanding in the scientific community and receiving remarkable attention from the cosmetic market.

The reported results showed the economic potential of using the Anacardiaceae family species as a differentiated plant raw material of inhibitory action of tyrosinase enzyme and melanin synthesis and, consequently, as potential bleaching agents.

The small number of articles founded with species of the Anacardiaceae family used as skin whitening agents show the need for a continuous effort of researchers and cosmetic industries to expand the studies of these species and eventually lead to the development of an innovative cosmetic more effective and safer.

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