REVIEW

Nutrition: The future of melanoma prevention?

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Background: Melanoma is one of the deadliest forms of skin cancer, having a high metastatic potential and afflicting all age groups. The need for successful preventative measures is particularly urgent as metastatic melanoma is largely incurable. The beneficial role of nutrition and other natural compounds in the prevention and treatment of melanoma has been clearly demonstrated in the past, and is an exciting source for potential therapies in the future.

Objective: We sought to review updates in the current literature regarding new developments in the relationship between nutrition and melanoma risk and treatment.

Methods: Articles in the public domain regarding the impact of diet, grape seed proanthocyanidins, selenium, vitamin D, vitamin E, epigallocatechin-3-gallate, resveratrol, rosmarinic acid, lycopene, and fig latex on melanoma were included.

Results: Grape seed proanthocyanidins, epigallocatechin-3-gallate, resveratrol, rosmarinic acid, lycopene, and fig latex have demonstrated clear anticancer effects toward melanoma. The roles of selenium, vitamin D, and vitamin E, however, have been more controversial.

Limitations: None.

Conclusions: The role of natural compounds in the future of melanoma prevention and treatment is promising and one that is worthy of further exploration. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2014.01.910.)

Key words: melanoma; nutrition; prevention; resveratrol; skin cancer; vitamins.

Skin cancer is the most common of all cancers.[1] Melanoma is one of the deadliest forms of skin cancer, causing up to 9480 deaths a year because of its high metastatic potential.[1,2] Melanoma occurs in all age groups, and incidence has been rising despite efforts to improve sun protection, highlighting the need for additional preventative measures and treatment.[3]

Although early melanoma can usually be cured by surgical resection, metastatic melanoma is largely incurable. Consequently, recent interest in preventive methods, such as dietary factors, has grown significantly. Epidemiologic and basic science studies have shown promising results supporting the role of natural compounds in the chemoprevention of melanoma. The discovery of effective natural compounds against melanoma may have important public health ramifications. Furthermore, dietary interventions may have systemic benefits in comparison with topical methods of sun protection, and do not require regular reapplication.

Oxidative damage plays a key role in the development of melanoma; free radicals and reactive oxygen species are generated by ultraviolet (UV)

Abbreviations used:

EGCG:	epigallocatechin-3-gallate
GSP:	grape seed proanthocyanidin
RCT:	randomized controlled trial
UV:	ultraviolet

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light, causing oxidative stress, inflammation, photoaging, and DNA damage, which can lead to skin cancer.[4,5] Exposure to UV light is one of the most important factors in the development of both melanoma and nonmelanoma skin cancers, and is largely unavoidable, further underscoring the need to discover novel agents that can help reverse the consequences of this damage.[6,7] In this review, we discuss the relationship between nutrients and melanoma risk, specifically epigallocatechin-3-gallate (EGCG), selenium, grape seed proanthocyanidins (GSPs), vitamin D, vitamin E, diet composition, fatty acids, resveratrol, rosmarinic acid, lycopene, and fig latex.

CAPSULE SUMMARY

- Treatment of metastatic melanoma has been very difficult and expensive. Prevention is key in reducing the incidence of melanoma.
- A clear beneficial relationship has been demonstrated between nutrition and melanoma prevention.
- The role of nutrition in melanoma risk and treatment is one that deserves further exploration.

METHODS

From September to October 2013 we searched PubMed for published studies examining the effects of diet and nutrition on melanoma risk and treatment. PubMed database was searched using search terms "nutrition," "melanoma," "treatment," "risk," "skin cancer," and "prevention." These terms included the subcategories "skin neoplasms," "food," "nutritional status," "nutritional sciences," "therapy," "therapeutics," and "prevention and control." The searches were filtered to include only those written in English. Bibliographies were searched for additional studies that met inclusion criteria. A total of 87 articles were found and examined in this review.

Grades of evidence used to evaluate the existing data for each nutrient (Table I) were based on those set by the Institute for Clinical Systems Improvement.[8] Level Ia refers to evidence from meta-analysis of randomized controlled trials (RCTs); Ib refers to evidence from at least 1 RCT; IIa refers to evidence from at least 1 non-RCT; IIb refers to at least 1 experimental study; III refers to evidence from case, correlation, or comparative studies; and IV refers to evidence from expert opinions.

RESULTS

Diet

Dietary composition has been demonstrated to impact skin cancer risk. Polyunsaturated fatty acids in particular are thought to play a role in melanoma prevention by protecting against UV skin damage, promoting tumor latency, inhibiting tumor multiplicity, and reducing cutaneous p53 expression.[9] In a major study investigating the link between dietary fatty acids and melanoma involving 50,757 Norwegian men and women, higher intake of cod liver oil (odds ratio 2.9, 95% confidence interval 1.7-5.1) and polyunsaturated fats (odds ratio 4.1, 95% confidence interval 1.4-11.8) was found to increase the risk of melanoma in women.[10]

In a case-control study performed by Fortes et al,[11] shellfish, daily tea consumption, vegetables, and fish were found to have protective benefits. This may be a result in part of the high isoprenoid content found in fruits and vegetables, as isoprenoids are known to inhibit melanoma B16 cell proliferation.[12] Consequently, the Mediterranean diet, which has long been touted for its high concentration of fish and vegetables, was also shown to have chemopreventive effects against melanoma.[11] Other studies supporting the Mediterranean diet have demonstrated a higher percentage of subcutaneous tissue polyunsaturated fatty acids and linoleic acid in patients with melanoma versus control subjects.[13] Thus, diets supporting the use of vegetable oil and fish consumption have been recommended.[13]

Grape seed proanthocyanidins

GSPs are effective antioxidants and anti-inflammatory agents and are found in particularly high concentrations in grapes.[14-16] GSPs have been found to reduce UV skin damage, such as photoaging, and to decrease melanin synthesis.[17] In human beings, GSPs have been shown to reduce mutant p53-positive epidermal cells and prevents depletion of Langerhans cells after sunburn.[18]

Mouse studies have also shown strong evidence supporting the inhibition of UV-induced tumor incidence, growth, and size, as well as metastatic pulmonary nodules, after the administration of grape seed extract.[15,19] GSPs were also shown to inhibit cell migration in highly metastasis-specific human A375 and Hs294t melanoma cell lines: 22% to 65%, $P <$ .01 to .001 and 29% to 69%, $P <$ .01 to .001, respectively.[20] In addition, GSPs decreased tissue plasminogen activator–induced activation of extracellular-signal-regulated kinase 1/2 protein and nuclear factor-κB/p65. These proteins have been shown to enhance and mediate migration of