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THE ROLE OF LEGAL ADDICTIVE SUBSTANCES IN SKIN PATHOLOGIES: A LITERATURE REVIEW

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ABSTRACT

Introduction and Objective. The skin not only plays a fundamental role in protecting the body from external factors, but also participates in thermoregulatory, metabolic, immunological and sensory processes. More and more attention is being paid (both in the scientific community and among patients) to the impact of lifestyle, including the use of legal stimulants such as alcohol or products containing nicotine on the condition of the skin. The aim of this paper was to present the current state of knowledge regarding the impact of harmful, easily accessible and legal addictive substances on human skin and also to support an interdisciplinary approach to the prevention and treatment of skin pathologies associated with their use.
Review methods. The research was conducted as a literature review based on information obtained from PubMed, Embase, GoogleScholar using combinations of the following keywords: skin, cigarettes, alcohol, nicotine, lifestyle, substance, abuse, cancer.
The state of knowledge. Biological mechanisms through which alcohol and nicotine (in both traditional and e-cigarette forms) affect the condition of the skin include the induction of oxidative stress, microcirculation disturbances, modulation of the immune response and disruptions in collagen metabolism. These mechanisms influence wound healing, exacerbate the course of inflammatory skin diseases, contribute to the development of neoplastic lesions and accelerate the skin aging process. There are reports of potential therapeutic benefits of nicotine in certain dermatoses. However, researchers point out the methodological limitations in existing studies.
Conclusion. Alcohol and tobacco products have a negative impact on the skin – they disrupt microcirculation, weaken the epidermal barrier, slow down wound healing and accelerate aging. In the context of the growing popularity of e-cigarettes and alternative forms of nicotine consumption, the need for further, well-designed research in this area is emphasized.

KEYWORDS

Skin, Cigarettes, Alcohol, Substance Abuse, Cancer

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Introduction

The skin constitutes the largest organ of the human body, in an average adult, it weighs approximately 5 kg and covers up to 2 m². It is involved in vitamin D synthesis, thermoregulation, the reception of environmental stimuli, serves as a water reservoir (especially the hypodermis) and attachment sites for certain muscles. However the most important function of the skin is considered to be its protective function [1,2]. It is the first barrier between the body and external environment threats, while also reflecting the overall health and internal processes happening in the organism. In recent years, there has been a visible trend of greater concern about skin health, with increasing attention being paid not only to the positive effects of cosmetics but also to lifestyle factors, which include addictive substances [3,4]. While, for example, illegal drugs are generally rejected by most of the society, some substances—such as nicotine products and alcohol—are completely legal, widely accessible and socially accepted. Their prevalence in human customs, traditions and cultures does not change the fact that chronic use of them is associated with numerous health consequences, including dermatological ones [4].

The aim of this paper is to present the effects of widely accessible and commonly used substances in society on various aspects of human skin health. It will discuss the basic mechanisms of influence of alcohol and tobacco products on the condition of the skin, the course of selected diseases, the development of some skin cancers, and the aesthetic aspects of these changes. The following considerations are also intended to look at these stimulants from the perspective of positive changes, despite the pejorative connotation of the word "substance" in the language. The work is intended to facilitate a conscious approach to stimulants, which are the most often encountered, in the context of prevention and treatment of dermatological diseases.

Alcohol

Alcohol is one of the most commonly used psychoactive substances. It is estimated that as many as 1.03 billion men and 312 million women over the age of 15 consume alcohol in amounts that exceed the level considered to be safe [5]. On the one hand, one of the challenges in measuring the impact of alcohol on human health is the variety of forms and concentrations in which it may be consumed. On the other hand, its widespread use as well as the wide social acceptance of its consumption make it easier to find research groups compared to many other substances. Alcohol has a number of effects on the human body—it acts on the central nervous system, inducing euphoria, changing perception and motor skills at lower doses, and at higher doses, it can cause total intoxication and even death.The impact of alcohol on the largest human organism, the skin, is also significant [4].

The pathological processes occurring and manifesting in the skin which are the result of alcohol's action on the skin, are diverse. Alcohol disrupts repair processes occurring in various tissues of the human body: bones, muscles and mucous membranes. The production of cytokines and chemokines in the presence of this substance may negatively impact wound healing processes. It leads to increased oxidative stress, which affects DNA functions through the induction of epigenetic changes [6]. This substance is also a promoter of increased vascular permeability, which can cause harmless redness of the skin after consumption of the stimulant, but at the same time contributes to the development of inflammation of skin tissues [4].

The aforementioned pathomechanisms, due to the multifaceted nature of their action, are associated with many widespread skin diseases, which include: acne vulgaris, rosacea, psoriasis, atopic dermatitis or even skin cancers [7].

Acne vulgaris is one of the most common skin diseases. Alcohol is probably one of the factors influencing its prevalence (through its effect on the microorganisms present on the skin that convert alcohol into acetaldehyde), although the studies conducted so far are not conclusive [7,8]. The same applies to rosacea - the analyses in that case are not certain as well. Alcohol is believed to influence the course of this disease by dilating blood vessels, which facilitates the disease process and also by affecting the gut microbiota. The lack of consensus on the effects of alcohol in this case is probably due to its different effects on specific subtypes of the disease [7,9].

Psoriasis is a disease that often occurs with other pathological conditions in the body and is also a disease that is exacerbated by many different factors. Earlier studies suggested that the risk of psoriasis was increased with alcohol consumption in the mechanisms of increased inflammation and promotion of epidermal keratinocyte proliferation [10]. More recent studies are not so conclusive, for example epigenetic analyses have not shown a direct link between alcohol and the occurrence of psoriasis [7,11]. In another inflammatory skin disease, atopic dermatitis, a correlation has been observed between alcohol consumption by pregnant women and the occurrence of atopic dermatitis in their offspring [12]. In older age groups (i.e. among teenagers and adults) this effect is not that obvious and may depend on the amount of alcohol consumed [13].

The effect of alcohol on the health of human skin also involves neoplastic changes. In the case of melanoma numerous studies, including extensive meta-analyses, identify alcohol as one of the risk factors for the development of this tumor [14]. Particularly the consumption of white wine and strong alcohols is presented as strongly associated with this risk. As in the case of some non-cancerous diseases, the causes of this effect are thought to be the action of the ethanol metabolite - acetaldehyde and in disruptions in the proper functioning of the immune system [7]. These mechanisms are also factors that increase the chances of developing non-melanoma skin cancers such as squamous cell carcinoma and basal cell carcinoma. The same types of alcohols that are associated with melanoma are seen as the most likely to cause these neoplastic changes [15,16].

However, skin lesions resulting from alcohol consumption are not only limited to diseases that primarily affect skin tissues. Alcohol is a contributing factor in the development of diseases affecting the digestive system, metabolism or kidneys, which secondarily affects the condition of the skin. In the case of the digestive system, alcohol is one of the most common causes of liver cirrhosis. While symptoms such as spider angioma, palmar erythema, xanthelasma, jaundice and pigmentary alterations, hair and nail changes, bleeding and clotting defects are considered to be nonspecific symptoms and occur in cirrhosis of various origins, certain signs are more specifically associated with alcoholic cirrhosis—namely, "money skin" and Dupuytren's contracture [17]. Excessive alcohol consumption is also associated with the occurrence of metabolic disorders such as type 2 diabetes [18]. The characteristic skin manifestations of this disease include: acrochordons, eruptive xanthoma, xerosis, inflammatory skin diseases, acanthosis nigricans, skin tags, hyperkeratosis, psoriasis, lichen planus, necrobiosis lipoidica, bullosis diabeticorum, scleredema diabeticorum, diabetic dermopathy, rubeosis faciei, granuloma annulare, vitiligo, onychomycosis, dermatophytosis, bacterial

infections (e.g., cellulitis, folliculitis, erythrasma) [19]. The connection between renal pathology and alcohol consumption in specific doses has been demonstrated in the course of, for example, chronic kidney disease [20]. In such case, skin changes can be divided into those not specific for chronic kidney disease, i.e.: generalized pruritus, xerosis, acquired ichthyosis, pigmentation changes, purpuric spots, nail and mucosal changes, cutaneous findings due to hormonal changes, and those more representative of the condition: perforating dermatoses, calciphylaxis, calcinosis cutis, bullous diseases, eruptive xanthoma, iododerma and nephrogenic systemic fibrosis (while only the latter is considered to be highly specific for CKD) [21].

The skin aging processes are also modulated to some extent by the presence of alcohol in the body. It has been shown that long-term alcohol consumption can accelerate the aforementioned processes. Research indicates that in people who abuse alcohol, telomere shortening may occur, which is a recognized marker of tissue aging [22]. Telomere shortening also contributes to the acceleration of the skin aging process, although it has also been shown that it can have a positive effect on the health of this organ by reducing the risk of developing cutaneous melanoma and non-melanoma skin cancers (NMSCs) [23].

Many skin pathologies that reflect disorders caused by excessive alcohol consumption can be considered indisputable and certain. On the other hand, its impact on the development and severity of some diseases can be considered to remain ambiguous. This state requires further analysis, taking into account factors such as: the amount and type of alcohol consumed, the severity of secondary disorders or the age of the individuals in the studied group [7].

Tobacco products and nicotine

The most recent WHO report from 2022 shows that there are 1.25 billion people worldwide who use tobacco products. This study had previously highlighted a noticeable trend - a decrease in the percentage of people using tobacco (currently one in five people, whereas in 2000, it was one in three). Concerning trends include the slow decline in tobacco use among specific groups (e.g., European women) or the demonstration of nicotine addiction among younger populations, i.e. aged 13–15 [21]. More recent studies conducted in Poland in 2024 revealed that 30.4% of adults declared smoking cigarettes within the past 30 days preceding the study, with 20.4% doing so daily. The prevalence of other nicotine delivery methods—such as e-cigarettes and heated tobacco—was also examined. In these cases, the statistics were as follows: in the last 30 days, 15.2% of respondents used e-cigarettes, and in the case of heated tobacco - 10.9%. When broken down by daily use, these numbers were 5.9% and 4.9%, respectively. Additionally, 10% of respondents used more than one form of tobacco products [25].

The most thoroughly studied group of tobacco products are cigarettes. When they are burned, toxic tobacco smoke is inhaled, which contains over 7,000 chemical substances, of which at least 250 are considered toxic and more than 70 are carcinogenic. The components of tobacco smoke include: nicotine, carbon monoxide, formaldehyde, acetaldehyde, acetone, benzene, cadmium and lead [26,27]. Most of the smoke is absorbed into the body through the respiratory tract, although some of it is absorbed through the skin and mucous membranes. Once these substances enter the bloodstream, they can cause harmful effects on various organs, including the skin [28].

The substances contained in cigarette smoke damage the skin barrier, increase transepidermal water loss and destroy the connective tissue of the skin [29]. Their effects on the connective tissue are twofold: on the one hand, cigarette smoke disrupts the production of collagen, on the other, it enhances the activity of matrix metalloproteinases which are responsible for collagen and elastic fibers degradation due interaction with the aryl hydrocarbon receptor [29,30]. It has been shown that cigarette smoking leads to problems in the homeostasis of skin proteins and lipids, even in areas that have not been directly exposed to smoke [31]. It has been proven that smoking causes an increase in the number of cells producing interleukin 17 in peripheral blood, as well as in other tissues, including the skin, which is responsible for promoting inflammation [5]. Nicotine contained in tobacco products causes vasoconstriction with accompanying local hyperemia. In contrast to tobacco smoke as a whole, it reduces the occurrence of inflammation by acting on both the central and peripheral nervous system and directly by affecting the cells of the immune system [32]. In general, cigarette smoking may contribute to disturbances in the thickness and density of the dermis and epidermis [33].

Some of the skin changes caused by smoking tobacco products are thought to be primarily aesthetic. The typical smoker's face is characterized by wrinkles and lines extending from the upper and lower lips and from the outer corners of the eyes, as well as numerous depressions in the cheek and jaw area. There is also a general emaciation of facial features with a more sharp outline of the contours of the facial bones lying under the skin tissue. The skin becomes atrophic, its colors change - it is described as grayish, though orange, purple

or red complexions are also seen as a result of hyperemia [34]. Common effects of smoking include discoloration of light-colored mustaches and nails near the burned cigarette, resulting from the action of coloring substances contained in cigarette smoke. If a person quits smoking tobacco in the form of cigarettes, a line may appear on the nail plate, separating the discoloured nail from the one that has not been in contact with harmful substances [35]. Such nails are called Harlequin or quitter's nails [36]. The temperature generated during cigarette burning also affects the condition of the skin, causing discolouration as a result of post-inflammatory hyperpigmentation [35].

In vivo studies have shown that smoking cigarettes contributes to premature skin aging and have helped to identify which factors at the molecular level are the essence of this process [35,37]. Skin aging is accelerated by oxidative stress, loss of collagen and activation of genes associated with aging - for example p16INK4a is mentioned here. Both active and passive smoking affect fibroblasts, accelerate their aging and, ultimately, damage the skin [29]. Even skin protected from sun exposure—another harmful factor—but still exposed to cigarette smoke experiences degradation of its elastic fiber network, leading to increased rigidity of the dermis and epidermis. These changes seem to be partially responsible for the loss of skin elasticity and the formation of wrinkles, which are indicators of skin aging [30]. The appearance of already existing wrinkles is exacerbated by cigarette smoke, which dehydrates the stratum corneum of the epidermis and causes a mild inflammatory reaction [35]. However, if we were to combine the two factors mentioned above (i.e. exposure to sunlight for more than 2 hours per day and smoking cigarettes defined as 35 pack-years), the harmful effect on the skin becomes even more severe - the risk of developing wrinkles is 11.4 times higher than in those who avoid these factors [38]. The number of pack-years and the number of cigarettes smoked are important - in studies, smoking more than 40 packs of cigarettes per year was considered to be extremely harmful [36]. There are some noticeable gender differences in the effect of smoking on skin aging, although women and men are equally prone to the development of elastosis, men are more likely to develop telangiectasia caused by smoking [39]. A particularly clear example of accelerated skin aging as a result of addiction to tobacco products is a study conducted on a pair of twins with similar risk factors, differing only in smoking status. It was found that a smoker with 52.5 pack-years showed significantly more pronounced signs of aging than a non-smoker [40]. If we take into account just nicotine itself, a molecule with a wider occurrence than only cigarettes, it turns out that it itself affects the skin aging process. This occurs as a result of vasoconstriction, damage to the vascular endothelium and probably the previously mentioned disorders of collagen synthesis and keratinocyte pathology [32].

Cigarette smoking prolongs wound healing time mainly due to the toxic effects of hydrogen cyanide, carbon dioxide and nicotine. Hydrogen cyanide and carbon dioxide impair tissue oxygenation processes. Nicotine is responsible for vasoconstriction, the occurrence of coagulopathies and the reduction of oxygen supply to tissues. As a result of these processes the healing of post-traumatic, post-operative and disease-related wounds is impaired which may lead to infection, wound dehiscence or local tissue necrosis [36,41]. Even short-term smoking cessation prior to surgery has a positive effect on the healing process, such wounds are less likely to become infected, although this does not apply to all types of complications [42]. A large meta-analysis involving over 218,000 patients showed that smokers were much more likely to experience postoperative complications, such as delayed wound healing, necrosis or infections, compared to never smokers or those who had quit smoking. Notably, the latter group, even many years after quitting smoking, continued to exhibit negative effects of smoking, although to a lesser extent than active smokers [43].

The course of many chronic dermatoses is modulated by cigarette smoking. Meta-analyses have shown a link between smoking and the incidence of psoriasis, with a positive correlation between the number of cigarettes smoked, the duration of smoking and the incidence of the disease. Moreover, people with psoriasis were found to smoke more often [44]. Some studies have shown that smokers respond less effectively to antipsoriatic medications, though this has not been confirmed by all research [45]. Similar inconsistencies occur in the case of hand eczema - some data suggest that smoking may increase its incidence, while other studies are inconclusive [46]. Due to the presence of numerous allergens in cigarettes, e.g. formaldehyde and menthol, they are presumed to be a potential risk factor in the development of allergic contact dermatitis [36]. One of the skin disorders most strongly correlated with smoking is palmoplantar pustulosis - around 95% of affected individuals are smokers, particularly heavy smokers. In this group, an abnormal response to nicotine is observed, which is probably the basis of the disorder [35]. In the case of skin appendages such as hair, in addition to the previously mentioned discoloration, a significant intensification of androgenetic alopecia has been observed [35,47]. Hidradenitis suppurativa also shows a correlation between its frequency and smoking, as well as with the severity of symptoms [48,49]. Cutaneous lupus erythematosus occurs more often in smokers,

while patients with discoid lupus erythematosus may experience a more acute onset of symptoms, and antimalarial drugs used in the treatment of this disease tend to be less effective in smokers [35,36]. Discrepancies in studies on the effects of tobacco smoking have been noted in the course of acne vulgaris [36]. Some studies prove that it worsens the condition and increases its frequency, while others suggest that smoking may have an anti-inflammatory effect in this disease, especially in young female populations—though they strongly discourage smoking as a form of treatment [50,51].

Smoking increases the risk of developing at least 17 types of cancer, including cancers of the lungs, oral cavity, oropharynx, nasopharynx, hypopharynx, esophagus (adenocarcinoma and squamous-cell carcinoma), stomach, colorectum, liver, pancreas, nasal cavity and paranasal sinuses, larynx, lung, uterine cervix, ovary (mucinous), urinary bladder, kidney, ureter, and bone marrow (myeloid leukemia) [52]. However, the situation regarding the influence of smoking on the development of skin cancers is not so definitive. In non-melanoma skin cancers, an increased risk of developing cutaneous squamous cell carcinoma has been proven, but the same has not been shown for basal cell carcinoma [53]. Furthermore, meta-analyses have provided evidence that in active smokers (this did not apply to people who smoked but stopped) the risk of developing such cancer is actually reduced [54]. A similar protective effect has been observed in melanoma - it was proven that cigarette smoking reduced the risk by 41% in men and by 20% in women when compared to people who had never smoked [55].

In addition to the negative effects of smoking, nicotine has been found to have an anti-inflammatory effect by activating α7 nAChR receptors, which inhibit the production of inflammatory cytokines and free radicals, while supporting the secretion of anti-inflammatory cytokines such as IL-10 and TGF-β [35]. Some therapeutic properties of nicotine have been noted in the course of Buerger's disease - despite a strong correlation with cigarette smoking, the use of nicotine chewing gum has been found to be helpful in treatment [56]. Similarly, in Behçet's disease, aphthous lesions may worsen upon quitting smoking, while nicotine use alleviates symptoms, probably by inhibiting the secretion of inflammatory cytokines. The use of transdermal nicotine has also proven helpful in modulating the course of diseases such as Degos disease, pyoderma gangrenosum, erythema nodosum [35].

Studies examining the effect of nicotine products on the condition of the skin have thus far focused on cigarette smoking or smoking tobacco in other forms and have been studied in many dimensions. A new challenge for the health of human skin appears to be the use of e-cigarettes, once presented as a healthier alternative to smoking. However, studies on e-cigarettes also provide evidence that they are a risk factor for the development of diseases such as psoriasis. Vaping, on the other hand, has been found to impair proper wound healing and cause thermal burns. The insufficient number of studies and the growing popularity of using this type of stimulants present themselves as a promising area for deeper scientific investigation [57].

Conclusions

The skin reflects the state of internal health, and cutaneous changes can be the first symptom of pathological processes occurring in the human body. These changes may be limited only to the skin itself, which does not necessarily mean that they are less dangerous. Legal stimulants, such as alcohol and products containing tobacco, have a proven negative effect on skin health. They disrupt microcirculation, the epidermal barrier function and immune processes, contributing to the development of many skin pathologies. Alcohol promotes skin dehydration and exacerbates the course of inflammatory diseases such as rosacea or psoriasis, and is also associated with a higher risk of certain skin cancers, especially in people who drink chronically and in large quantities. Smoking can delay wound healing, increase the risk of postoperative infections, tissue necrosis and impair collagen synthesis. E-cigarettes, despite being once perceived as a "safer alternative", also have a negative effect on the skin condition, although there is still much to be researched in this field. While there are isolated reports of potential beneficial effects of nicotine in some dermatological conditions, the possible benefits do not outweigh the health risks associated with the use of nicotine-containing products. As more and more research is conducted, there is a need for more in-depth analysis of the effects of legal stimulants on the skin, especially in the context of the growing popularity of new forms of their consumption, such as e-cigarettes.

Disclosure

Author's Contribution

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