REVIEW ARTICLE

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Effect of cannabis usage on the oral environment: a review

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© 2008 The Authors. Journal compilation © 2008 Blackwell Munksgaard **Abstract:** *Aim:* To evaluate oral environmental changes in cannabis users. *Material and Methods:* The MEDLINE and Cochrane Central register of controlled trails (CENTRAL) were searched up to April 2007 to identify appropriate studies. *Results:* Independent screening of 982 titles and abstracts (MEDLINE-Pubmed) and (Cochrane) papers resulted in seven eligible publications. *Conclusion:* Based on the limited data, it seems justified to conclude that with increasing prevalence of cannabis use, oral health care providers should be aware of cannabis-associated oral side effects, such as xerostemia, leukoedema and an increased prevalence and density of *Candida albicans.*

Key words: cannabis usage; oral environment; review

Introduction

Cannabis is a drug of plant origin and is abused worldwide. The plant has been grown and cultivated since the beginning of civilization for fibre and as a source of medicine (1). Until 500 AD, its use as a mind-altering drug was almost solely confined in India. In the twentieth century, there was a rise in the use of cannabis for recreational and religious purposes. Cannabis contains a unique group of chemicals, namely cannabinoids, some of which are psychoactive (2). There are three main forms of cannabis: marijuana, hash and hashoil.

Smoking marijuana is the most common and efficient way of using cannabis as it is easy to prepare and its effects are rapid (1, 3). The immediate effect of smoking cannabis is the creation of a pleasant, dreamy state, with impairment of attention, cognitive and psychomotor performance, which appears to the subject to be reversible. The effects of cannabis depend on the potency of the drug, the manner used and quantity and past cannabis experience (4). Because of its lack of acute life-threatening effects, cannabis has been called a 'soft drug', no more damaging than coffee or tobacco, but it has both acute and chronic adverse effects (5).

9-tetrahydrocannabinol (THC) is the main source of the pharmacological effects caused by the consumption of cannabis. Cannabis affects almost every system of the body, particularly the cardiovascular, respiratory and immune systems. Medically, cannabis is most often used as an appetite stimulant and pain reliever for certain illnesses, such as cancer, AIDS and other diseases. It is used to relieve glaucoma and certain neurological illnesses, such as epilepsy, migraine and bipolar disorder. However, despite these potential benefits (medical applications of cannabis), the non-medical use of cannabis can have adverse effects on the general and mental health of users, particularly, when used regularly for an extended period of time (2). It is known that traces of THC are still present in the brain 24 h after administration (6). THC also has a direct effect on immune cell activity. THC has an immunosuppressive effect on macrophages, natural killer cells, T and B lymphocytes. This results in decreased host resistance to bacterial and viral infections (7, 8). Smoking cannabis provides a chronic inflammation of the oral mucosa (9). This change in the oral mucosa may result from the high temperature of the inhaled smoke and/or from the specific chemicals contained in the smoke (10). Gingival and periodontal effects, such as a fieryred gingivitis, leukoplakia on the gingiva, gingival inflammation, gingival hyperplasia and alveolar bone loss have been documented as a result of chronic use of cannabis (for review see: 4, 11). Colon (12) reported multiple cases of oral papillomas occurring in heavy cannabis users. Baddour et al. (9) describe a case of a diffuse chronic hyperplastic gingiva being related to the smoking of cannabis. Guarisco et al. (13) reported on three cases of the oral manifestation of isolated uvulitis secondary to cannabis inhalant irritation. Cannabis smoking has also been suggested as a possible cause of tongue carcinoma (14). Cannabis abusers generally have poorer oral health than non-users, with an increased risk of dental caries and periodontal diseases (10). The purpose of the present review was to evaluate in a systematic manner the oral environmental effects in cannabis users.

Material and Methods

Literature search

Two internet sources of evidence were selected in search of appropriate papers for this study purpose: the National Library of Medicine, Washington, DC (MEDLINE: PubMed) and the Cochrane Central register of controlled trails. This search was performed to be inclusive for any study which evaluated the effect of cannabis usage on the oral environment.

The database was searched up to and including April 2007. The following terms were used for both search strategies: (Intervention)

[MESH terms] 'CANNABIS' or 'MARIJUANA ABUSE' or 'MARIJUANA SMOKING' or 'CANNABINOIDS' or 'ENDOCANNABINOIDS' or 'EDESTIN PROTEIN' or 'CANNABIS SATIVA' OR [TEXT words] cannabis OR marijuana abuse OR marijuana smoking OR cannabinoids OR endocannabinoids OR edestin protein OR *Cannabis sativa* OR marihuana OR marijuana OR weet OR hash OR feruloyltyramine OR tetrahydrocannabinol OR cannabinol OR cannabidiol OR *p*-coumaroyltyramine OR Soft drugs

AND

(Outcome)

[MESH terms] 'PATHOLOGY, ORAL' or 'SOFT TISSUE INFECTIONS' or 'CANDIDA' or 'HALITOSIS' or 'ORAL HYGIENE INDEX' or 'ORAL HEALTH' or 'ORAL HYGIENE' or 'MOUTH' or 'PERIODONTAL DISEASES' OR [TEXT words] oral pathology OR soft tissue infections OR *Candida* OR halitosis OR oral hygiene index OR oral health OR oral hygiene OR mouth OR periodontal disease* OR periapical abcess OR periodontitis juvenile OR periapical periodontitis OR periodontitis OR gingival disease* OR gingival inflammation OR gingivitis OR periodontitis OR oral tissue OR dry mouth OR xerostomia OR periodontium.

Eligibility criteria

Screening was performed independently by two reviewers (GAW and PAV). At first they screened by title and abstract. Then as a second step, full text papers were obtained when they fulfilled the eligibility criteria for inclusion related to the study aim.

For full text screening, the following criteria were taken into consideration:

- Randomized Controlled Trials
- Controlled Clinical Trials
- Cohort Study
- Intervention: cannabis usage
- In humans

Only studies written in English language were accepted. Case reports, letters and historical reviews were not accepted in the search. Studies without abstracts of whose title suggested that they were related to the objectives of this review were also selected so that the full text could be screened for eligibility. All reference lists of the selected studies were screened for additional papers which would meet the eligibility criteria for the study. Any disagreements between the reviewers were resolved by discussion.

Results and Discussion

Search results

The MEDLINE-PubMed search resulted in 457 abstracts and the Cochrane search in 536 abstracts with 111 duplicates (Table 1). After screening these 982 abstracts by title and abstract, 8 papers were selected for full-reading after which 1 paper had to be excluded as this was a review. Screening of the reference lists of the seven selected studies resulted in no additional papers. An overview of the papers and the study characteristics are presented in Table 2. The study outcomes in relation to various oral environmental changes are presented in Tables 3–7.

Xerostomia

The results of a study by Darling and Arendorf (15; Table 2: #1) showed that the prevalence of a dry mouth after smoking cannabis was significantly greater when compared with the cigarette-smoking controls (69.6% and 18.6%, respectively, P < 0.001) (Table 3). Cannabis is a drug with parasympatholytic properties and hence can produce the clinical symptom of xerostomia (16–19). The prevalence of caries and periodontal disease may therefore be increased in cannabis abusers (11).

Weller and Halikas (20; Table 2: #6) determined the changes that occur in the acute and hang-over effects experienced by individuals who have used cannabis for 5–6 years (Table 6). They found in 97 regular cannabis users not only a statistically significant decrease in pleasurable effects but also some undesirable effects. The oral side effect of a dry mouth and throat (on a scale from 0 = once or never, 1 = occasionally and 2 = usually) decreased from 1.60 to 1.47 (P < 0.025). So possibly some degree of tolerance had developed in 5–6 years.

Table 1. Search results

Selection	PubMed	Cochrane	Identical
Search Excluded: titles and abstracts	457 449	536 536	111 111
Selected papers for full reading Excluded from selection after full reading		8 1	
Included of reference lists Subfinal selection Final selection for data extraction		- 7 papers	

Leukoedema

Leukoedema is a common developmental alteration of the oral mucosa which appears to be a simple variation of normal anatomy. It appears as a filmy, opaque, white to slate grey discolouration of mucosa, chiefly buccal mucosa. Redundancy of the mucosa may impart a folded or wrinkled appearance to the relaxed mucous membrane. It partially disappears when the mucosa is stretched which aids to differentiate this lesion from other similar looking conditions which could be premalignant, such as leukoplakia.

Darling and Arendorf (15; Table 2: #1) concluded that leukoedema occurred more frequently in cannabis users than in non-smokers (57.1% and 20.2%, respectively) (P < 0.001) (Table 3). It has been suggested that leukoedema is a condition which partly results from repeated and low-grade irritation to the oral mucosa (21). Many relate the presence of leukoedema to habits, including smoking (21–25), cheek sucking (25) betel nut chewing (22) and coca leaf chewing (26). Van Wyk & Ambrosio (27) suggest that leukoedema is a pathological entity and that cellular damage results in manifestation of the lesion. They further speculate that there is a threshold for smoking and when exceeded, leukoedema develops.

Oral cancer

The mechanism by which cannabis smoke may act as a carcinogen relates to the presence of aromatic hydrocarbons, benzopyrene and nitrosamines (14, 28) in amounts 50% greater than the same amount of tobacco smoke (29). Smoking cannabis is associated with oral premalignant lesions, including leukoplakia and erythroplakia (30). The association between cannabis use and head and neck cancer was stronger among younger patients (<50 years old) (31) and more aggressive (14).

In two separate case–control studies, Llewellyn *et al.* (32; Table 2: #2) (33; Table 2: #3) examined the risk factors for oral cancer in recently diagnosed patients aged 45 years and found no significant risk for cannabis use (Table 4). In a large case-controlled study (n = 407 cases), Rosenblatt *et al.* (34; Table 2: #4) conducted a study to determine whether cannabis use is associated with the development of oral squamous cell carcinoma in 18–65 years old patients. They found that there was no association with ever having used cannabis (OR = 0.9; 95% CI: 0.6–1.3).

Plaque and gingivitis

Silverstein *et al.* (10; Table 2: #5) examined the effects of highcannabis-use on the oral environment (Table 5). A group of 206

Table 2.	Overview o	f the studies processed for	r data extrac	tion		
Study number	Ref number	Author(s), year	Design	Title	Intervention/Comparison	Conclusion
÷	Ω	Darling MR and Arendorf TM (1993)	ССТ	Effects of cannabis smoking on oral soft tissues	Marijunana smokers/non-smokers and tobacco smokers	Significant difference between lesions and conditions in cannabis users and controls occurred with respect to leukoedema, dry mouth, traumatic ulcer
# 2	32	Llewellyn CD <i>et al.</i> (2004a)	CCT	An analysis of risk factors for oral cancer in young people: a case-control study	Squamous cell carcinoma/subjects who never had cancer	No significant risks were found
θ #	33	Llewellyn CD <i>et al.</i> (2004b)	ССТ	Risk factors for oral cancer in newly diagnosed patients aged 45 years and younger: a case-control study in Southern England	Squamous cell carcinoma/subjects who never had cancer	Non-significant odds ratio was found for cannabis use even after adjusting for tobacco and alcohol habits
# 4	34	Rosenblatt KA <i>et al.</i> (2004)	ССТ	Marijuana use and risk of oral squamous cell carcinoma (OSCC)	Oral squamous cell carcinoma/ no diagnose of oral squamous cell carcinoma	Marijunana use was not associated with oral squamous cell carcinoma risk
ب #	0	Silverstein SJ <i>et al.</i> (1978)	CCT	Social drug use/abuse and dental disease	Marijunana smokers/no experience with social drug use and vegetarianism	The high-cannabis-use group had a greater number of decayed, missing and filling teeth, a greater accumulation of plaque and a greater severity of gingivitis than a comparable group of non-drug users
9 #	20	Weller RA and Hallikas, JA (1982)	Follow-up	Change in effects from marijuana: a five- to six-year follow-up	Marijuana smokers/no comparison	Decreases found in undesirable effects such as dry mouth raised the possibility that some degree of tolerance had developed
2 #	35	Darling MR <i>et al.</i> (1990)	CCT	Effect of cannabis use on oral candidal carriage	Marijuana smokers $(n = 55)/tobacco$ smokers $(n = 58)/non-smokers$ (n = 50)	Cannabis smoking significantly increases the prevalence of oral carriage of <i>Candida albicans</i>
UCT COT	oinio pallorio	al trials. SCC scillamore	ll carcinoma:		a	

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Table 3. Occurence of leukoedema and dry mouth by percentage in cannabis/methaqualone/tobacco smokers (CMT), cigarette smoking controls and non-smoking controls

#1	CMT smokers	Cigarette smoking controls	Non-smoking controls
Number	266	145	168
Mean age	24.7	28.3	25.3
Mean duration cannabis smoking years	8.9	_	_
Mean duration of cigarette smoking (years)	6.9	9.2	_
Leukoedema	57.1%	51.7%	20.2%
Significance difference of leukoedema	4		*
Dry mouth after smoking Significance difference of dry mouth	69.6%	18.6%	Not assessed

 \bullet *CMT smokers versus non-smokers, chi-squared, P < 0.001.

 \bullet [†]CMT smokers versus cigarette smokers, chi-squared, P < 0.001.

high-cannabis-use subjects living in a commune was selected as the study population (82% of the subjects had used cannabis \geq 1000 days). The results indicate that the non-use group had substantially lower number of decayed, filled or missing surfaces (DMF-S scores), lower plaque scores, healthier gingiva (Table 5). So it can be concluded that cannabis users had a poorer oral health condition which most likely reflects their lifestyle with a neglect of health in general (10).

Candida albicans

Darling *et al.* (35; Table 2: #7) studied the effect of cannabis smoking on oral candidiasis as well as the oral prevalence and density of *C. albicans* using an imprint culture technique. They demonstrated an increased prevalence of *C. albicans* in cannabis users when compared with tobacco-smoking and non-smoking controls. There was no apparent difference in the prevalence of candidiasis (Table 7). The increasing number and density of *C. albicans* can be because of the presence of hydrocarbons of cannabis which acts as an energy source for certain *Candida* species. Additional factors such as compro-

Table 4.	Risk of	oral	cancer	associated	with	use of	cannabis
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Table 5. Comparison of a high-cannabis-use group to a non-drug-use group

	High-marij	uana-use	Non-drug-	·use	
	group (n =	= 206)	group (n =	= 68)	
#5	Mean	SD	Mean	SD	
Age	25.5	3.4	26.8	5.0	
DMF-S^	26.2	18.7	20.5	18.8	
Plaque*	2.82	1.26	1.93	1.23	
Gingivitis [†]	0.83	0.39	0.31	0.27	

^DMF-S (decayed, missing, filled surfaces).

*Personal Hygiene Performance-index (PHP) as described by Martens & Meskin (37).

[†]Dental Health Centre-index (DHC) as described by Smith (38).

Table 6. Acute effects of cannabis intoxication (n = 97)

#6	Initial	Follow-up
Dry mouth and throat	1.60	1.47*

*Statistically significant P < 0.025.

Table 7. Candidal prevalence: (a) comparison between CMT, C1 and C2, showing presence and absence of *Candida* on subjects (CMT: n = 55, C1: n = 50, C2: n = 58); (b) comparison between CMT, C1 and C2

#7	Abse	nt	Present	
(a) CMT C1 C2	11 (3 32 (6 33 (4	8.2) 4.0) 6.9)	34 (61.8) 18 (36.0) 25 (43.1)	
#7	CMT versus C1	CMT versus C2	C1 versus C2	
(b) Chi-square	<i>P</i> = 0.008	<i>P</i> = 0.047	<i>P</i> = 0.452	

CMT = cannabis/methaqualone/tobacco smokers, C1 = nonsmoker controls, C2 = tobacco-smoking controls. Values are given in n (%).

mised immune response because of chronic use of cannabis, poor denture hygiene and nutritional factors should also be considered (35).

Conclusion

Based on the limited data, it seems justified to conclude that with increasing prevalence of cannabis use (36), oral health

Study number	Cases	Controls	OR (95% CI)	♂ OR (95% CI)	♀ OR (95% CI)
#2, Cannabis user	n = 116, 13%	n = 207, 10%	1.0 (0.5–2.2)*	0.9 (0.4–2.2)*	1.7 (0.4–7.0)*
#3, Cannabis user	n = 53, 9%	n = 91, 15%	0.3 (0.1–1.8)*	0.3 (0.1–3.9)*	0.7 (0.1–184.9)*
#4, Cannabis user	n = 407, 25.6%	n = 615, 24.4%	0.9 (0.6–1.3)	–	–

*Estimates from conditional regressions analysis for alcohol and tobacco consumption. Odds ratios (OR) and corresponding 95% confidence intervals (CI). care providers should be aware of cannabis-associated oral side effects, such as xerostemia, leukoedema and an increased prevalence and density of *C. albicans.*

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