

# Primena etarskog ulja čajnog drveta u stomatologiji

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## The application of Tea tree essential oil in dentistry

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### KRATAK SADRŽAJ

*Etarska ulja imaju široku primenu u medicini, stomatologiji i kozmetologiji, kao korigensi ukusa i mirisa različitih sredstava za oralnu higijenu. Cilj ovog rada je bio da se kroz analizu aktuelnih naučnih i stručnih publikacija sveobuhvatno prikažu mogućnosti primene etarskog ulja *Melaleuca Alternifolia* u stomatologiji. Primena etarskog ulja čajnog drveta u lečenju parodontopatije, gljivičnih oboljenja, kao i u terapiji virusnih infekcija, se pokazala izuzetno efikasnom. Ispitivanjem antimikrobnog dejstva deset različitih etarskih ulja, potvrđeno je da je etarsko ulje čajnog drveta vrlo efikasno protiv niza Gram + i Gram - bakterija. In vitro ispitivanja bakteriostatskog, baktericidnog i fungicidnog delovanja rastvora ulja čajnog drveta na deset različitih mikroorganizama su potvrdila osetljivost sledećih mikroorganizama: *Actinobacillus actinomycetemcomitans*, *Fusobacterium nucleatum* i *Porphyromonas gingivalis*, i nešto slabije prema bakterijama *Streptococcus Mutans* i *Prevotella intermedia*. Čajno drvo se pokazalo izuzetno blagotvornim u lečenju različitih oboljenja i predstavlja uvod i podstrek za primenu biljnih preparata u lečenju brojnih manifestacija kod različitih oboljenja u stomatologiji.*

Lekovito bilje se vekovima primenjuje u profilaksi i lečenju mnogih oboljenja. Zahvaljujući dejstvu svojih aktivnih principa ali i zbog svoje blagotvornosti i efikasnosti, preparati na bazi lekovitog bilja su sve zastupljeniji u savremenoj fitoterapiji.<sup>1</sup> Razvojem eksperimentalne farmakognozije ovi preparati dobijaju i naučnu potvrdu o svojoj delotvornosti, pa danas, u svetu medicine i stoma-

### SUMMARY

*Essential oils are widely used in medicine, dentistry and cosmetology as flavour and odour corrigents in various substances for oral hygiene. The aim of this study was to present comprehensively the possibilities for application of *Melaleuca Alternifolia* essential oil in dentistry based on the analysis of contemporary scientific and professional publications. The application of Tea tree essential oil in the treatment of periodontal, fungal and viral diseases is very efficient. The study of antimicrobial potential of ten different essential oils confirmed the efficiency of Tea tree oil against numerous Gram+ and Gram- bacteria. In vitro studies of bacteriostatic, bactericidal and fungicidal effect of Tea tree oil solution against ten different microorganisms confirmed sensitivity of the following microorganisms: *Actinobacillus actinomycetemcomitans*, *Fusobacterium nucleatum* and *Porphyromonas gingivalis*, and slightly weaker effect against *Streptococcus Mutans* and *Prevotella intermedia*. Tea tree is very effective in the treatment of various diseases and is an introduction and momentum for the application of plant substances in the treatment of numerous diseases in dentistry.*

Herbal medications have been used in the prevention and treatment of many diseases for centuries. Thanks to their active ingredients, their beneficialness and efficiency, herbal medications are more and more present in contemporary phytotherapy.<sup>1</sup> With the development of experimental pharmacognosia, these substances gain scientific confirmation of their potential. In today's world of

tologije postoji sve veći interes za njihovu primenu upravo zbog terapijskog efekta zasnovanog na potpuno prirodnoj osnovi.

Etarska ulja su isparljivi, mirisni sastojci, koji predstavljaju složene mešavine alifatičnih i aromatičnih, terpenkih i fenil-propanskih jedinjenja. Glavni i najzastupljeniji sastojci etarskih ulja su terpeni i seskviterpeni<sup>2</sup>, koji predstavljaju polimere izoprena dobijene prema opštem izoprenskom pravilu koje je formulisao Otto Wallach.<sup>3</sup>

U stomatologiji se naročito primenjuje lekovito bilje sa etarskim uljima kao korigens ukusa i mirisa, različitih sredstava za održavanje oralne higijene kao što su paste za zube i vodice za ispiranje usta.

Poznato je da etarska ulja mogu imati i blago antivirusno i antibakterijsko dejstvo.<sup>1</sup> Tako se na primer ulje eukaliptusa, nane, i čajnog drveta dodaju preparatima za otklanjanje neprijatnog zadaha i dezinfekciju oralne sluzokože.<sup>1</sup>

Cilj ovog rada je bio da se kroz analizu aktuelnih naučnih i stručnih publikacija sveobuhvatno prikažu mogućnosti primene etarskog ulja *Melaleuca Alternifolia* u stomatologiji.

## Aktivni principi i antimikrobno delovanje etarskog ulja čajnog drveta

Još tridesetih godina XX veka, dokazana je klinička efikasnost etarskog ulja čajnog drveta u različitim medicinskim indikacionim područjima. U jednom od prvih publikovanih radova u stručnim medicinskim časopisima, Penfold i Morrison su objavili su da je etarsko ulje čajnog drveta 11 do 13 puta efikasnije u uništavanju bacila tifusa od karbolne kiseline, koja je do tada primenjivana.<sup>7</sup> Penfold je 1938.god. ispitivao efekat rastvora etarskog ulja čajnog drveta na površine inficiranih rana i ustanovio da je nakon terapije došlo do eliminacije zapaljenja bez vidljivog oštećenja tkiva.<sup>7</sup>

Sredinom sedamdesetih godina ispitivanjima terapijske efikasnosti čajnog drveta posvećuje se sve veća pažnja.

Etarsko ulje čajnog drveta predstavlja izrazito lipofilnu supstancu. Način njegovog dejstva objašnjava se postojanjem lipofilnog terpena (terpinen-4-ol), jednog od najznačajnijih aktivnih principa ovog etarskog ulja. Terpinen-4-ol prodire u ćelijsku membranu mikroorganizama i deluje na njenu strukturu tako što utiče na njenu permeabilnost. Na ovaj način etarsko ulje čajnog drveta može uticati na metabolizam nekih mikroorganizama i ispoljiti baktericidno ili fungicidno dejstvo.<sup>4-6</sup>

Iako sastav etarskog ulja čajnog drveta koji obezbeđuje optimalnu antimikrobnu aktivnost nije u potpunosti definisan, postoje snažni dokazi da je terpinen-4-ol, monoterpenski alkohol, najznačajnija komponenta ovog etarskog ulja. Tako su Williams, Southwell i Griffin ustanovili da antimikrobna aktivnost signifikantno raste kako se koncentracija terpinen-4-ol-a povećava do 40% u etarskom

medicine and dentistry, there is a growing interest in their application due to their therapeutic effect based on entirely natural grounds.

Essential oils are volatile, odoured substances made up of complex mixture of aliphatic and aromatic, terpinen and phenyl-propane compounds. Main ingredients of essential oils are terpenes and sesquiterpenes<sup>2</sup> that are polymers of isoprene obtained according to the general isoprene rule defined by Otto Wallach.<sup>3</sup>

In dentistry, herbal medicines with essential oils are especially used as flavour and odour corrigents in many substances for oral hygiene such as toothpastes and mouthrinses.

It is known that essential oils may possess mild antiviral and antibacterial effect.<sup>1</sup> For example, eucalyptus and tea tree oils are added to substances against bad breath and disinfectants of oral mucosa.<sup>1</sup>

The aim of this paper was to present comprehensively the possibilities for application of *Melaleuca Alternifolia* essential oil in dentistry based on the analysis of contemporary scientific and professional publications.

## Active ingredients and antimicrobial potential of tea tree essential oil

During the 1930-ties, clinical efficacy of Tea tree essential oil was confirmed in different medical indications. In one of the first published articles in foreign medical journals, penfold and Morrison reported that Tea tree essential oil was 11-13 times more efficient against typhus bacilli than carbolic acid which had been used until then.<sup>7</sup> In 1938, Penfold studied the effect of Tea tree essential oil on open wounds and found the elimination of inflammation without visible tissue damage after treatment.<sup>7</sup>

In mid70-ties there was a growing interest for the study of therapeutic efficiency of Tea tree.

Tea tree essential oil is an extremely lipophilic substance. Its mechanism is explained with lipophilic terpene (terpinen-4-ol), one of the most important active principles of this essential oil. Terpinen-4-ol enters microorganism cell membranes and acts against its structural permeability. In this way, Tea tree essential oil can affect the metabolism of certain microorganisms with bactericidal or fungicidal effect.<sup>4-6</sup>

Even though the composition of Tea tree essential oil that provides optimal antimicrobial activity is still fully uncovered, there is strong evidence that terpinen-4-ol, a monoterpene alcohol, is the most important component. Williams, Southwell and Griffin have found that antimicrobial activity significantly rises as the terpinen-4-ol concentration increases up to 40% in the essential oil.<sup>7</sup> ISO standard 4730 "Oil of *Melaleuca Ter-*

ulju.<sup>7</sup> ISO Standard 4730 «Oil of Melaleuca Terpinen-4-ol Type» (International Standard Organisation 1996) preporučuje minimalnu koncentraciju od 30 % terpinen-4-ol-a pa do 40 % kao komponente u etarskom ulju čajnog drveta.<sup>7</sup>

Posljednjih godina dosta pažnje posvećeno je i 1,8 cineolu, kao još jednom od aktivnih principa etarskog ulja čajnog drveta. Standardom je određena maksimalna koncentracija 1,8 cineola od 15 %. Etarska ulja sa nižim nivoom terpinen-4-ol-a pokazuju manju antimikrobnu aktivnost. S obzirom da postoji stalna tendencija u smanjivanju nivoa cineola u etarskom ulju, dobijena su etarska ulja čajnog drveta sa niskim nivoom cineola (manje od 5 %), a višim nivoom terpinen-4-ol-a. Smatra se da ova ulja imaju najbolju antimikrobnu aktivnost.<sup>7</sup>

Jedan od prvih naučnih radova o antimikrobnom dejstvu etarskog ulja čajnog drveta publikovan je od strane Low et al. (1974), kada je prikazano dejstvo etarskog ulja čajnog drveta na različite sojeve mikroorganizama. Antimikrobna efikasnost izražena u vrednostima minimalno inhibitorne koncentracije-MIC (Minimal Inhibitory Concentration) iznosila je 1:16 za *Staphylococcus Aureus* i 1:32 za *Salmonella Typhi*.<sup>7</sup>

U velikoj studiji Beylier-a (1979) koja se bavila ispitivanjem antimikrobnog dejstva deset različitih etarskih ulja, etarsko ulje čajnog drveta pokazalo se vrlo efikasnim protiv niza Gram + i Gram - bakterija.<sup>7</sup> U tabeli 1. sistematizovani su rezultati različitih relevantnih studija i prikazan je spektar antimikrobne aktivnosti etarskog ulja čajnog drveta sa vrednostima MIC (Minimal Inhibitory Concentration)<sup>7</sup>

pinen-4-ol Type» (International Standard Organisation 1996) recommends minimal concentration of terpinen-4-ol between 30% and 40% as a component in Tea tree essential oil.<sup>7</sup>

In recent years, much attention has been paid to 1,8 cineol as another active principle of Tea tree essential oil. Maximum concentration of 1,8 cineol is recommended to be 15%. Essential oils with lower levels of terpinen-4-ol exhibit lower antimicrobial activity. Given the fact that there is a tendency in decreasing cineol levels in essential oils, Tea tree essential oils with lower cineol (less than 5%) and higher terpinen-4-ol levels have been produced. It is believed that these oils have the best antimicrobial activity.<sup>7</sup>

One of the first scientific papers on antimicrobial effect of Tea tree essential oil was published by Low et. al (1974) reporting the effect of Tea tree essential oil against different microbial species. Antimicrobial efficacy, given in MIC (Minimal Inhibitory Concentration) values, was 1:16 against *Staphylococcus Aureus* and 1:32 against *Salmonella Typhi*.<sup>7</sup>

In a large study of Beylier (1979) the antimicrobial effect of ten different essential oils was examined, with Tea tree essential oil being very efficient against various Gram+ and Gram- bacteria.<sup>7</sup> Table 1 presents the results of various relevant studies with the spectrum of antimicrobial activity of Tea tree essential oil with MIC values.<sup>7</sup>

Tabela 1. Spektar antimikrobne delatnosti etarskog ulja čajnog drveta

Table 1. The spectrum of antimicrobial activity of Tea tree essential oil

MIKROORGANIZMI	REFERENCE	MIC %(V/V) K-si mb.
<b>Gram pozitivne bakterije</b>		
<i>Staphylococcus aureus</i>	A,b,c,d,e,h(105),j(69),k	0,2
MRSA	g(60),k	0,2-0,3
<i>Staphylococcus epidermidis</i>	C,e,j(15),k	0,5
<i>Enterococcus faecalis</i>	K	0,5
<i>Propionibacterium acnes</i>	B,e,f(32),k	0,4-0,5
<i>Micrococcus lutens</i>	J(4),k	0,2
<i>Corynebacterium spp.</i>	J(10),k	0,2-0,3
<i>Bacillus subtilis</i>	K	0,3
<i>Bacillus cereus</i>	K	0,3-0,4
<i>Streptococcus spp.</i>	L	
<b>Gram negativne bakterije</b>		
<i>Escherichia coli</i>	A,b,c,d,h(110),k	0,2
<i>Enterobacter aerogenes</i>	K	0,3
<i>Klebsiella pneumoniae</i>	J(13),k	0,3
<i>Proteus vulgaris</i>	K	0,2
<i>Pseudomonas aeruginosa</i>	A,c,j(10),k(3)	>2
<i>Pseudomonas putida</i>	K	0,5

MIKROORGANIZMI	REFERENCE	MIC %(V/V) K-si mb.
<i>Serratia marcescens</i>	J(11),k	0,2-0,3
<i>Legionella pneumophila</i>	K	
<b>Gljivice</b>		
<i>Candida</i> spp	A,b,c,d,j(15),k,l(32)	0,2
<i>Malassezia furfur</i>	l(52),m(22)	
<i>Pityosporum orales</i>	J	0,2
<b>Plesni</b>		
<i>Aspergillus niger</i>	A,d,k	0,3-0,4
<i>Aspergillus flavus</i>	B,k	0,4-0,5
<i>Trychophyton mentagrophytes</i>	B,k,m	1
<i>Trychophyton rubrum</i>	B,k,m	

1- brojevi u zagradama odnose se na broj testiranih izolata

2- a Beylier (1979); b Besset et al (1990); c Williams et al(1993); d Sauthwell et al (1993); e Raman et al (1995); f Carson and Riley (1994); g Carson et al (1995a); h Carson et al (1995b); i Hammer (1996); j Hammer et al (1996); k Griffin et al (1998); l Carson et al (1996); m Nenoff et al (1996).

1- numbers in brackets refer to the number of tested isolates

2- a Beylier (1979); b Besset et al (1990); c Williams et al(1993); d Sauthwell et al (1993); e Raman et al (1995); f Carson and Riley (1994); g Carson et al (1995a); h Carson et al (1995b); i Hammer (1996); j Hammer et al (1996); k Griffin et al (1998); l Carson et al (1996); m Nenoff et al (1996).

U brojnim *in vitro* testovima dokazano je snažno antibakterijsko dejstvo čajnog drveta protiv mnogih mikroorganizama kao sto su : *Salmonella typhi*, *Staphylococcus aureus* i drugih bakterija iz roda *Staphylococcus*, zatim *Escherichia coli*, *Proteus vulgaris*, *Enterococcus* spp., *Enterobacter* spp., *Streptococcus* spp., *Branhamella catarrhalis*, *Mycobacterium smegmatis*, *Clostridium perfringens*, *Lactobacillus acidophilus*, *Bacteroides fragillis*, *Bacillus subtilis*, kao i protiv drugih G+ i G- bakterija. Antigljivično dejstvo dokazano je protiv *Aspergillus niger* i *Candida albicans*. MIC (Minimal Inhibitory Concentration) procenjena je na oko 0,125 do 1 %.<sup>7</sup>

A number of *in vitro* studies have confirmed the powerful antimicrobial effect of Tea tree against various microorganisms such as: *Salmonella typhi*, *Staphylococcus aureus* and other *Staphylococcus* spp., *Escherichia coli*, *Proteus vulgaris*, *Enterococcus* spp., *Enterobacter* spp., *Streptococcus* spp., *Branhamella catarrhalis*, *Mycobacterium smegmatis*, *Clostridium perfringens*, *Lactobacillus acidophilus*, *Bacteroides fragillis*, *Bacillus subtilis*, as well as other G+ i G- bacteria. Antifungal activity was confirmed against *Aspergillus niger* and *Candida albicans*. MIC (Minimal Inhibitory Concentration) was cca 0,125 do 1 %.<sup>7</sup>

## Primena etarskog ulja čajnog drveta u stomatologiji

Usna duplja predstavlja sredinu koju normalno nastanjuje veliki broj različitih mikroorganizama. S obzirom na to da ovi mikroorganizmi žive na svim površinama usne duplje, u slučaju prekida ili smanjenja brige o higijeni usta i zuba, disbalansa u ishrani, kod opštih oboljenja ili usled dejstava nekog lokalnog faktora dolazi do poremećaja oralne homeostaze i stvaranja mogućnosti za razvoj različitih oboljenja ( karijes, parodontopatija, oralnu kandidiaza i HSV infekcije).

### Antikarijesno i antiplak dejstvo čajnog drveta

Razvoj dentalnog plaka direktni je etiološki faktor za nastanak gingivitisa i parodontopatije, a poremećaj higijensko-dijetetskog režima potvrđeni je faktor rizika za nastanak karijesa.<sup>8</sup>

## The use of tea tree essential oil in dentistry

Oral cavity is an environment normally inhabited by a number of different species of microorganisms. Given that these microorganisms live on all oral surfaces, cases of total absence or low oral hygiene levels, dietary imbalances, systemic diseases or local factors may result in an imbalance of oral homeostasis and various diseases (caries, periodontal disease, oral candidiasis and HSV infections).

### Anticariious and antiplaque effect of tea tree

The formation of dental plaque is an etiological factor for gingivitis and periodontal disease while the hygienic-dietary imbalance is a confirmed risk factor for caries occurrence.<sup>8</sup>

Hammer i sar. su ispitivali antimikrobnu aktivnost čajnog drveta na 162 bakterijske vrste. Pri koncentraciji 2% ili manjoj, ulje čajnog drveta je bilo efikasno na svaku bakterijsku vrstu. Sa najnižom minimalnom inhibitornom koncentracijom, MIC (Minimal Inhibitory Concentration) i minimalnom baktericidnom koncentracijom MBC (Minimal Bactericidal Concentration) eliminisana je *Prevotella*, *Porphyromonas* i *Veillonella*, a sa najvišom *Streptococcus*, *Fusobacterium* i *Lactobacillus*. Tretman sa 4%, 2%, 1% i 0,5% uljem čajnog drveta dovelo je do smanjenja broja mikroorganizama u kulturi, nakon samo 30 sec. tretmana. Takode, "viable cells" (žive bakterije koje su sposobne da rastu i razmnožavaju se), nisu bile nativne posle tretmana.<sup>8</sup>

Ispitivanja baktericidnog dejstva u različitim vremenskim intervalima ("Time kill" studije), na izolatima *Lactobacillus rhamnosus*, vrsti vezanoj za karijes zuba, pokazala su efikasnost 0,5% i 1%-tnog ulja čajnog drveta, dok je nešto manja efikasnost postignuta sa uljem koncentracije 0,25%. Studija u kojoj su Hammer i sar. 2003.god. ispitivali osetljivost bakterija na ulje čajnog drveta, ukazuje na to da bi upotreba ulja čajnog drveta u rastvorima za ispiranje usta svakako mogla biti efikasna u redukciji kariogenih vrsta kao što su *Streptococcus Mutans*, bakterije iz roda *Lactobacillus* i bakterije iz roda *Fusobacterium* u oralnoj sredini.<sup>8</sup>

U kliničkim studijama dokazano je da rastvori za ispiranje usta koji sadrže etarska ulja čajnog drveta svojim aktivnim principima deluju na kariogene bakterije *Streptococcus Mutans*, redukujući njihovo prisustvo u dentalnom plaku. Na taj način ovi rastvori pokazuju antikariogeno dejstvo slično onom koje pokazuje chlor-hexidine.<sup>9</sup>

### **Primena čajnog drveta u lečenju parodontopatije**

Kada se govori o parodontopatijama, veoma je značajno dejstvo čajnog drveta ne širok spektar oralnih mikroorganizama (Gram + i Gram - bakterija i gljivica).<sup>10</sup> U jednoj *in vitro* studiji posmatrano je bakteriostatsko, baktericidno i fungicidno delovanje rastvora ulja čajnog drveta na deset različitih mikroorganizama.<sup>10</sup> U ovom istraživanju korišćeni su sledeći preparati: rastvor ulja čajnog drveta, gel na bazi čajnog drveta za oralnu upotrebu (Tebodont®), Trager gel (gel nosač), Chlorhexidin rastvor i PlakOut® (koji sadrži 0,2% chlorhexidina). Vrednost MIC (minimalne inhibitorne koncentracije - Minimal Inhibitory Concentration) kod rastvora ulja čajnog drveta je bila od 0.0293% do 1,25%. Vrednost MFBC (minimalne baktericidno-fungicidne koncentracije, Minimal Bactericidal and Fungicidal Concentration) iznosi 0,0521% i 2,5% za rastvor ulja čajnog drveta i 0,0098%- 3,33% za gel na bazi čajnog drveta za oralnu upotrebu. Najosetljivijim su se pokazali sledeći mikroorganizmi: *Actinobacillus actinomycetmcomitans*, zatim *Fusobacterium nucleatum* i *Porphyromonas gingivalis*, dok najslabije dejstvo preparati čajnog drveta ispoljavaju prema bakterijama *Streptococcus Mutans* i *Prevotella intermedia*.<sup>10</sup>

Hammer et al. have investigated the antimicrobial activity of Tea tree against 162 bacteria species. At 2% or lower concentration, Tea tree essential oil was efficient against every bacterial species. With the lowest minimal inhibitory concentration, MIC and minimal bactericidal concentration, MIC, *Prevotella*, *Porphyromonas* and *Veillonella* were eliminated while *Streptococcus*, *Fusobacterium* and *Lactobacillus* were eliminated with the highest. Treatments with 4%, 2%, 1% and 0.5% Tea tree essential oil resulted in decrease in the number of microorganisms in the culture, after only 30 s of treatment. Furthermore, "viable cells" (living bacteria that are capable of growing and mitosis) were not native after the treatment.<sup>8</sup>

Studies of bactericidal effect after various time periods ("Time kill" studies) on *Lactobacillus rhamnosus* isolates, a caries-related species, confirmed the efficiency of 0.5% and 1% Tea tree essential oil while slightly lower efficiency was observed with 0.25% Tea tree essential oil. A study by Hammer et al. (2003), who investigated bacterial sensitivity against Tea tree essential oil, suggested that the use of Tea tree essential oil in mouthrinses could be efficient in the reduction of cariogenic species, such as *Streptococcus Mutans*, *Lactobacillus* and *Fusobacterium spp.*<sup>8</sup>

In clinical studies, it has been confirmed that mouthrinses with Tea tree essential oil act against cariogenic bacteria, *Streptococcus Mutans*, reducing their presence in the plaque. In this way, these solutions show anti-cariogenic effect similar to the one of chlorhexidine.<sup>9</sup>

### **The use of tea tree essential oil in the treatment of periodontal disease**

Speaking of periodontal disease, Tea tree effect against a wide spectrum of oral microorganisms (Gram+ and Gram- bacteria and fungi) is very important.<sup>10</sup> An *in vitro* study tested bacteriostatic, bactericidal and fungicidal effect of Tea tree essential oil against ten different microorganisms.<sup>10</sup> The following substances were used in this study: Tea tree essential oil solution for oral use (Tebodont®), Trager gel (carrier gel), Chlorhexidine solution and PlakOut (containing 0.2% chlorhexidine). MIC (Minimal Inhibitory Concentration) values for Tea tree essential oil solution was between 0.0293% and 1.25%. MFBC (Minimal bactericidal-fungicidal concentration) was 0.0521-2.5% for Tea tree essential oil solution and 0.0098-3.33% for Trager gel. The most sensitive microorganisms were *Actinobacillus actinomycetmcomitans*, *Fusobacterium nucleatum* and *Porphyromonas gingivalis*, while Tea tree medications showed the weakest effect against *Streptococcus Mutans* and *Prevotella intermedia*.<sup>10</sup>

U tabeli 2. su prikazani rezultati istraživanja Kulika i sar. koji govore o bakteriostatskom i baktericidnom dejstvu rastvora ulja čajnog drveta i rastvora gela na bazi ovog ulja na testirane mikroorganizme. Rezultati su izraženi preko izmerenih vrednosti MIC i MBFC.<sup>10</sup>

Table 2 presents the results of Kulik et al. study on bacteriostatic and bactericidal effect of Tea tree essential oil solution and gel solution against certain microorganisms. The results are presented in the form of MIC and MFBC values.<sup>10</sup>

Tabela 2. Prosečne minimalne baktericidne/fungicidne koncentracije

Table 2. Average minimal bactericidal/fungicidal concentrations

Mikroorganizmi	TTO rastvor	TTO gel	Gel (nosač)	PlakOut ®	Chlorhexidin
S. mutans	1,0417	3,33	N	0,0006	0,0016
S. sanguis	0,4167	0,625	N	<0,0005	0,0011
S. anginosus	0,4167	0,5208	N	<0,0005	0,0008
A. actinomycetemcomitans	0,0521	<0,0098	0,5208	<0,0002	0,0003
L. salivarius	1,5625	0,7292	N	<0,0002	<0,0004
A. naesludi	0,5208	1,25	N	<0,0002	<0,0004
F. nucleatum	0,1693	0,1172	0,1693	<0,0002	<0,00065
P. intermedia	2,5	1,875	N	0,0123	0,0125
P. gingivalis	0,0651	0,013	0,117	0,1027	0,0016
C. albicans	0,3125	0,2084	N	0,0018	0,0032

Kulik i sar. su upoređivanjem svojih rezultata sa rezultatima istraživanja Shapira i sar. (1994), Walsh & Longstaff-a (1987) došli do zaključka da gel sa etarskim uljem čajnog drveta predstavlja povoljan alternativni produkt u terapiji infekcija oralne sluzokože i parodontopatije. Njihove *in vitro* studije samo su podsticaj i uvod za dalja klinička istraživanja.<sup>10</sup>

#### Antiinflamatorno dejstvo čajnog drveta

U svom istraživanju, Soukulis i Hirsch 2004.god. su se bavili antiinflamatornim i antibakterijskim dejstvom etarskog ulja čajnog drveta.<sup>11</sup> U studiji je korišćeno 2,5% ulja čajnog drveta u eksperimentalnoj grupi, 0,2 % chlorhexidine je korišćen u pozitivnoj kontrolnoj grupi, a placebo u negativnoj kontrolnoj grupi. Antibakterijsko i antiinflamatorno dejstvo čajnog drveta procenjivano je gingivalnim indexom (Gingival Index –GI), indexom krvarenja gingive (Parodontal Bleeding Index- PBI) i indexom dentalnog plaka (Plaque Surface Score- PSS). Statistički značajna razlika dobijena je u grupama gde je tretman izvršen gelom na bazi ulja čajnog drveta u poređenju sa kontrolnim grupama (Chlorhexidine i Placebo) a dobijene su i niže vrednosti PBI i GI.

U ovom istraživanju vrednosti PSS indexa nisu bile statistički značajno promenjene, što praktično znači da antibakterijski efekti ulja čajnog drveta dolaze do izražaja u *in vitro* studijama.<sup>11</sup> Međutim, u *in vivo* studijama kao što je ova, primena ulja čajnog drveta ne utiče značajno na formiranje dentalnog plaka. Smanjenje gingivalne inflamacije kod

Comparing their results with the results of Shapiro et al. (1994) and Walsh & Longstaff (1987), Kulik et al. concluded that gel with Tea tree essential oil was an efficient alternative product in the treatment of oral mucosa infections and periodontal disease. Their *in vitro* studies are a momentum and introduction for further clinical studies.<sup>10</sup>

#### Anti-inflammatory effect of tea tree

In their study, Soukulis and Hirsch (2004) investigated anti-inflammatory and antibacterial effect of Tea tree essential oil.<sup>11</sup> In this study, 2.5% Tea tree essential oil was used in the experimental groups, 0.2% chlorhexidine as positive control and placebo as negative control. Antibacterial and anti-inflammatory effect of Tea tree was evaluated using gingival index (GI), periodontal bleeding index (PBI) and plaque surface score (PSS). There was a statistically significant difference between experimental and control groups with lower PBI and GI values. In this study, PSS values were not significantly different suggesting that antibacterial effect of Tea tree essential oil was evident in *in vitro* studies.<sup>11</sup> However, in *in vitro* studies such as this one, Tea tree essential oil has no influence on the formation of dental plaque. The reduction of gingival inflammation in patients using Tea tree essential oil without dental plaque decrease sug-

pacijenta koji su koristili ulje čajnog drveta bez smanjenja količine dentalnog plaka pokazuje da je mehanizam dejstva ulja čajnog drveta više anti-inflamatoran nego antibakterijski. Izrazito antiinflamatorno dejstvo etarskog ulja čajnog drveta dokazano je u mnogim *in vitro* i *in vivo* studijama.<sup>12-15</sup>

### **Antimikotično dejstvo**

*Candida Albicans*, gljivica koja normalno postoji u ljudskom telu i živi u ravnoteži sa ostalim mikroorganizmima, pod nekim uslovima može početi da buja i tada predstavlja patogenu vrstu. Najčešći uzrok nastanka kandidiaze jeste upotreba antibiotika koji eliminišu bakterije za šta se i koriste, ali i «prijateljske» *Lactobacille* koji normalno održavaju nivo Candide pod kontrolom.<sup>16</sup> Slično se događa i u trudnoći, usled pada imuniteta, hormonskih disbalansa ili loše ishrane (rigorozne dijeta). Pušači, dijabetičari i pacijenti koji nose parcijalne i totalne proteze, takode često oboljevaju od kandidijaze.<sup>16</sup>

Vazquez i Zawawi, opisuju efikasnost 2 rastvora, koja su sadržala čajno drvo, u lečenju infekcija usta i grla izazvanih *Candidom Albicans*, tj orofaringealne kandidiaze kod pacijenata obolelih od AIDS-a.<sup>17</sup> U njihovu studiju bilo je uključeno 27 pacijenata od kojih je 13 pacijenata primalo alkoholni, a 14 pacijenata bezalkoholni rastvor čajnog drveta. Nakon 4 nedelje primene rastvora, tj ispiranja (4 x dnevno 30-60 sec.), dva pacijenta iz alkoholne grupe i 4 pacijenta iz bezalkoholne grupe bilo je izlečeno. Kod 8 pacijenata u alkoholnoj grupi i 2 pacijenta u bezalkoholnoj grupi, došlo je do poboljšanja stanja za 60%. Ovim istraživanjem potvrđen je antimikotički potencijal ulja čajnog drveta što predstavlja podstrek za dalja ispitivanja.<sup>17</sup>

Jandourak i sar. su ispitivali efikasnost rastvora ulja čajnog drveta na kandidiazu kod pacijenata obolelih od AIDS-a. U studiju je bilo uključeno 13 pacijenata sa fluconazol-rezistentnom orofaringealnom kandidiazom. Rezistencija na fluconazol kod ovih pacijenata prethodno je potvrđena klinički i *in vitro*. Pacijenti su ispirali usta sa 15ml rastvora čajnog drveta 4 puta dnevno, 2 do 4 nedelje. Ova studija pokazala je da je rastvor etarskog ulja čajnog drveta efikasan čak i kod pacijenata obolelih od AIDS-a sa orofaringealnom kandidiazom rezistentnom na fluconazol.<sup>18</sup>

### **Antivirusno dejstvo čajnog drveta**

Do sada najmanje ispitivana osobina etarskog ulja čajnog drveta jeste njegovo antivirusno dejstvo. Kada se govori o oralnim virusnim infekcijama, jedna od najčešćih jeste infekcija humanim *Herpes simpleks* virusima tip 1 i 2.<sup>19</sup>

Terapija kako primarnih, tako i povratnih infekcija herpes virusima najčešće je simptomatska i podrazumeva primenu antipiretika i multivitaminsku ishranu, kao i lokalnu primenu antiseptika i antimikotika. Kauzalna terapija Aciklovirom se primenjuje sistemski najčešće kod imuno-kompromitovanih osoba ili teških rekurentnih formi herpesa a lokalno se kod odraslih primenjuje u vidu krema.<sup>19</sup>

Terpeni, konstituenti u hemijskom sastavu etarskog ulja čajnog drveta, omogućavaju njegove antimikrobne

gested that the mechanism of Tea tree essential oil was more anti-inflammatory than antibacterial. Significant anti-inflammatory effect of Tea tree essential oil was confirmed in many *in vitro* and *in vivo* studies.<sup>12-15</sup>

### **Antimicotic effect**

*Candida Albicans*, fungus normally found in a balance with other microorganisms in the human body may start to proliferate into a pathogenic species under certain conditions. The most common cause of candidiasis is the use of antibiotics to eliminate bacteria, which also eliminates "friendly" *Lactobacillus* spp. that normalize the levels of *Candida*.<sup>16</sup> Similar thing occurs during pregnancy due to immunity drop, hormone imbalance and improper nutrition (rigorous diets). Smokers, diabetics and patients with partial or total prosthesis often have candidiasis.<sup>16</sup>

Vazquez and Zawawi described the efficiency of two solutions containing Tea tree in the treatment of oral and pharyngeal infections caused by *C. albicans* i.e oropharyngeal candidiasis in AIDS patients.<sup>17</sup> Their study included 27 patients, 13 having alcohol-based and 14 non-alcohol-based Tea tree solution. After 4 weeks of treatment i.e rinsing (4 x per day for 30-60 s), two patients from the alcohol and 4 from non-alcohol group were cured. In 8 patients in the alcohol and 2 patients in non-alcohol group, there was 60% improvement. This study confirmed antimicotic potential of Tea tree essential oil which is a stimulant for further investigation.<sup>17</sup>

Jandourak et al. studied the efficiency of Tea tree essential oil solution in the treatment of candidiasis in AIDS patients. The study comprised 13 patients with fluconazol-resistant oropharyngeal candidiasis. Fluconazol resistance was previously confirmed clinically and *in vitro*. Patients rinsed mouth with 15 ml Tea tree essential oil solution 4 times daily for 2-4 weeks. This study showed that Tea tree essential oil solution was efficient even in patients with AIDS having fluconazol-resistant oropharyngeal candidiasis.<sup>18</sup>

### **Antiviral effect of tea tree**

The least investigated effect of Tea tree essential oil so far is its antiviral activity. Regarding human oral infections, one of the most common is Human simplex virus infection type 1 and 2.<sup>19</sup>

The treatment of primary as well as recurrent herpes simplex infections is mostly symptomatic and includes the use of antipyretics and multivitamin diet with local application of antiseptics and antimicrobics. Causal therapy with Acyclovir is systemically conducted in immuno-compromized persons or hard recurrent forms of herpes and locally in adults in the forms of cream.<sup>19</sup>

Terpenes, constituents in the chemical composition of Tea tree essential oil, enable its antimicrobial effects,

efekte, dok je laboratorijskim testovima na kulturi tkiva potvrđeno i postojanje antivirusnih efekata.<sup>20</sup> U pilot studiji (20 pacijenata), aplikovanjem 6% etarskog ulja čajnog drveta u gelu 5 puta dnevno, u okviru terapije labijalnog herpesa, postignuto je poboljšanje, iako nije dobijena statistička značajnost.<sup>20</sup>

Rezultati *in vitro* ispitivanja kojima je dokazana antivirusna aktivnost etarskog ulja čajnog drveta upućuju na nove mogućnosti lečenja infekcija izazvanih *Herpes simplex* virusima. U svom radu Schnitzler i sar. (2001.) su saopštili da jednočasovna izloženost etarskom ulju čajnog drveta koncentracije 0,0008% i 0,0009%, smanjuje formiranje kolonija virusa HSV1 i HSV2 na 50%.<sup>21</sup> Takođe, u drugom istraživanju, isti autori su poredili antivirusnu aktivnost eukaliptusovog ulja i ulja čajnog drveta. Etarsko ulje čajnog drveta, pokazalo je oko 10 puta veću antivirusnu aktivnost od eukaliptusovog ulja.<sup>21</sup>

Antivirusna aktivnost čajnog drveta svakako se ogleda u delovanju protiv velikog broja kliničkih izolata HSV 1. Rezultati naučne studije Carsona i sar.(2005) pokazali su da se opstanak virusa tretiranih sa etarskim uljem čajnog drveta kreće između 0,001 i 0,45 % . U okviru ovog istraživanja dokazano je virucidno dejstvo 2% etarskog ulja čajnog drveta protiv 14 kliničkih izolata HSV 1.<sup>22</sup>

S obzirom da se primena etarskog ulja čajnog drveta u nekim *in vitro* ispitivanjima pokazala efikasnom i ispoljila virucidno dejstvo, smatra se da ovo etarsko ulje poseduje veliki potencijal za lečenje infekcija izazvanih herpes virusima .

## Zaključak

Čajno drvo se pokazalo izuzetno blagotvornim u lečenju različitih oboljenja. Njegovi efekti su poznati kako kroz istoriju, a danas takođe postoji sigurna tendencija vraćanju prirodi i prirodnim preparatima. Uprkos lekovitom potencijalu ove biljke, do sada je objavljen mali broj radova koji ukazuju na mnogobrojne mogućnosti primene etarskog ulja čajnog drveta. Ovaj rad predstavlja samo uvod u buduća klinička i laboratorijska istraživanja i podstrek vraćanju primeni biljnih preparata u lečenju različitih infektivnih oboljenja u stomatologiji.

while antiviral effects have been confirmed in laboratory tests on cell cultures.<sup>20</sup> In a pilot study (20 patients), the application of 6% Tea tree essential oil gel 5 times daily as the treatment of labial herpes resulted in an improvement even though not statistically significant.<sup>20</sup>

The results of *in vitro* studies that prove antiviral activity of Tea tree essential oil imply new possibilities for treatment of HSV infections. In their paper, Schnitzler et al (2001) reported that 1 hour exposure to 0.0008% and 0.0009% Tea tree essential oil reduces the formation of HSV1 and HSV2 colonies.<sup>21</sup> In another study, the same authors compared the antiviral activities of eucalyptus oil and Tea tree oil. Tea tree essential oil showed cca 10 times higher antiviral activity than eucalyptus oil.<sup>21</sup>

Antiviral activity of Tea tree is proved against numerous clinical isolates of HSV1. The results of a study by Carson et al. (2005) revealed that only 0.001-0.45% viruses treated with Tea tree essential oil survived. In the same study, a virucidal effect of 2% Tea tree essential oil against 14 clinical isolates of HSV1 was proved.<sup>22</sup>

Given that the application of Tea tree essential oil in certain *in vitro* studies proved to be efficient with a virucidal effect, it is believed that essential oil possesses great potential for HSV infections.

## Conclusion

Tea tree is proved to be efficient in the treatment of various diseases. Its effects are known through history and today, there is a strong tendency to return to the nature and natural substances. In spite of a medical potential of this plant, a small number of articles has been published indicating numerous possibilities for the use of Tea tree essential oil. This paper is only an introduction for future clinical and laboratory investigation and a momentum for return to herbal medications in the treatment of different infective diseases in dentistry.

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