










# Unlocking the secrets of saliva: the promising potential of salivary biomarkers for evaluating crack use

Desvendando os segredos da saliva: o potencial promissor dos biomarcadores salivares para avaliar o uso de crack

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## ABSTRACT

The forthcoming letter will encompass the following highlights: Crack cocaine use involves smoking a highly addictive form of cocaine, which is a significant concern in Brazil, particularly in urban areas. This addiction is linked to various health problems, including cardiovascular issues, sexually transmitted infections (STIs) like AIDS and syphilis, tuberculosis, and a notable increase in mortality, largely due to violent causes. Furthermore, crack cocaine users are particularly vulnerable to dental caries, gingival inflammation, oral mucosa lesions, and xerostomia

## KEYWORDS

Crack Cocaine; Oral Health; Quality of Life; Body Fluids; Biomarkers.

## RESUMO

A próxima carta incluirá os seguintes destaques: O uso de crack envolve fumar uma forma altamente viciante da cocaína, o que é uma preocupação significativa no Brasil, especialmente em áreas urbanas. Esta dependência está ligada a vários problemas de saúde, incluindo problemas cardiovasculares, infecções sexualmente transmissíveis (IST), como a AIDS e a sífilis, a tuberculose e um aumento notável da mortalidade, devido, em grande parte, a causas violentas. Além disso, os usuários de crack são particularmente vulneráveis a cáries dentárias, inflamação gengival, lesões na mucosa oral e xerostomia.

## PALAVRAS-CHAVE

Cocaína Crack; Saúde Bucal; Qualidade de Vida; Líquidos Corporais; Biomarcadores

Crack cocaine use involves smoking a highly addictive form of cocaine, leading to intense but short-lived euphoria and severe health consequences [1]. Crack consumption in Brazil is a major concern, particularly in urban areas [2]. High addiction rates associated with extreme social consequences, such as poverty, violence and crime, pose significant public health challenges [3]. Moreover, crack/cocaine addiction is related to several health problems, such as cardiovascular problems, sexually transmitted infections (STIs), especially AIDS and syphilis, tuberculosis and a significant increase in mortality, especially due to violent causes [1,2]. Its ability to affect cognitive functioning has been documented [1]. While crack abuse is a global issue, Brazil is considered the world's second largest crack consumer market [4]. As a result, the referred scale and the specific socio-economic factors in Brazil differentiate it from other countries and demands targeted interventions [1-4].

In the oral cavity, there are many adverse effects associated with the use of crack on oral health-related quality of life [5], such as temporomandibular disorders due to bruxism, which can also cause tooth wear, jaw pain and headaches, leading to further oral health issues [6-8], increase in decayed, missing and filled teeth, especially due to the acidic properties of crack cocaine vapor which causes erosion of the tooth enamel, resulting in cavities and tooth decay overtime [9-11]. In addition to rupture of the periodontium, the vasoconstrictive properties of crack cocaine reduce blood flow to the gums, weakening the tissue and making it more susceptible to infection, leading to gum recession, bad breath, and, if left untreated, tooth loss [6,9,12]. It can cause injury to the oral mucosa, "dry mouth", oral burns, sores on the lips and inside the mouth due to the high temperatures and chromosomal breakage of cells in the oral mucosa [6,9,13]. In addition to difficulty swallowing and speaking, opportunistic fungal infections, periodontal disease in advanced stages and hyposalivation can also occur [9-14].

Biological fluids contain proteins and other molecules that can be used as biomarkers to detect the presence of psychoactive substances ("drug testing") [15,16], patterns of consumption [17] or to function as indicators of physiological processes or diseases, such as those related before or in response to a therapeutic agent [15,16,18]. Saliva, a transparent watery fluid secreted by the salivary glands directly into the oral cavity which contains

more than 2,000 proteins and peptides involved in a variety of different oral biological functions, is an excellent diagnostic fluid [16]. These proteins and peptides can be characterized and analyzed to monitor or identify various diseases by proteomic analysis in crack addicts [17].

Considering drug testing, saliva offers several advantages over urine for crack cocaine use, such as more comfort for the individual, thus preserving the individual's privacy and dignity during the testing process [19]. The saliva collection is easier, simpler, less intrusive than urine collection and has a reduced adulteration risk [20]. In addition, saliva tests can detect recent drug use, typically within a few hours to a couple of days. It provides more real-time information regarding drug exposure compared to urine tests, which have a longer detection window [21]. Detecting recent drug use may be crucial in various settings and situations where timely intervention is necessary [19-21].

Crack cocaine users are especially vulnerable to dental caries, gingival inflammation, oral mucosa lesions and xerostomia [15-17]. Salivary biomarkers, due to their non-invasive nature and ability to detect drug metabolites, have shown promising potential for evaluating both crack cocaine use itself and some of its main complications, such as cancers and periodontal diseases [15,16]. They offer a convenient and accessible method for monitoring drug exposure, assessing treatment progress and conducting research on drug use patterns. Saliva-based tests can provide real-time or recent drug use information and might help in early detection of crack cocaine abuse, intervention, and support for individuals struggling with addiction [17]. Further research and validation are needed to establish the reliability and accuracy of these biomarkers in specific contexts [15-17].

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## Author's Contributions

SSM: Substantial contributions to the conception and final approval of the version to be published. TMC: Conception of the letter, substantial contributions to the conception and final approval of the version to be published.

GRZ: Substantial contributions to the conception, drafting of the article, translation and final approval of the version to be published. FS: Critical review, final approval of the version to be published. HSM: Critical review, final approval of the version to be published. JDA: Conception of the letter, revising it critically for important intellectual content and final approval of the version to be published. MRA: Substantial contributions to the letter, revising it critically for important intellectual content and final approval of the version to be published.

## Conflict of Interest

No conflicts of interest declared concerning the publication of this article.

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## Regulatory Statement

None.

## REFERENCES

- Butler AJ, Rehm J, Fischer B. Health outcomes associated with crack-cocaine use: systematic review and meta-analyses. *Drug Alcohol Depend.* 2017;180:401-16. <http://dx.doi.org/10.1016/j.drugalcdep.2017.08.036>. PMID:28982092.
- Ribeiro M, Perrenoud LO, Duailibi S, Duailibi LB, Madruga C, Marques ACPR, et al. The Brazilian drug policy situation: the public health approach based on research undertaken in a developing country. *Public Health Rev.* 2013;35(2):7. <http://dx.doi.org/10.1007/BF03391706>.
- Ribeiro M, Duailibi S, Frajzinger R, Alonso AL, Marchetti L, Williams AV, et al. The Brazilian 'Cracolândia' open drug scene and the challenge of implementing a comprehensive and effective drug policy. *Addiction.* 2016;111(4):571-3. <http://dx.doi.org/10.1111/add.13151>. PMID:26497639.
- Abdalla RR, Madruga CS, Ribeiro M, Pinsky I, Caetano R, Laranjeira R. Prevalence of cocaine use in Brazil: data from the II Brazilian national alcohol and drugs survey (BNADS). *Addict Behav.* 2014;39(1):297-301. <http://dx.doi.org/10.1016/j.addbeh.2013.10.019>. PMID:24455783.
- Antoniazzi RP, Zanatta FB, Ardenghi TM, Feldens CA. The use of crack and other illicit drugs impacts oral health-related quality of life in Brazilians. *Oral Dis.* 2018;24(3):482-8. <http://dx.doi.org/10.1111/odi.12786>. PMID:28949432.
- Brand HS, Gonggrijp S, Blanksma CJ. Cocaine and oral health. *Br Dent J.* 2008;204(7):365-9. <http://dx.doi.org/10.1038/sj.bdj.2008.244>. PMID:18408681.
- Riva R, Rotemberg E, Sanguinetti M, et al. Drug dependence, bruxism and temporomandibular disorders comparative analysis of two populations: nationwide sample and portal amarillo's population in treatment for problematic drug use. *Odontostomatologia [Internet].* 2014 [cited 2023 may 18]; 16(24):26-33. Available from: [http://www.scielo.edu.uy/pdf/ode/v16n24/en\\_v16n24a05.pdf](http://www.scielo.edu.uy/pdf/ode/v16n24/en_v16n24a05.pdf)
- Teoh L, Moses G. Drug-induced bruxism. *Aust Prescr.* 2019 Aug;42(4):121. <https://>.
- Nassar P, Ouanounou A. Cocaine and methamphetamine: pharmacology and dental implications. *Can J Dent Hyg.* 2020;54(2):75-82. PMID:33240367.
- Cury PR, Oliveira MGA, Andrade KM, de Freitas MDS, dos Santos JN. Dental health status in crack/cocaine-addicted men: a cross-sectional study. *Environ Sci Pollut Res Int.* 2017;24(8):7585-90. <http://dx.doi.org/10.1007/s11356-017-8404-z>. PMID:28120223.
- Antoniazzi RP, Palmeira RV, Schöffner C, Santos BZ, Zanatta FB, Feldens CA. Use of crack cocaine increases tooth loss. *Am J Dent.* 2021;34(6):317. PMID:35051319.
- Antoniazzi RP, Zanatta FB, Rösing CK, Feldens CA. Association among periodontitis and the use of crack cocaine and other illicit drugs. *J Periodontol.* 2016;87(12):1396-405. <http://dx.doi.org/10.1902/jop.2016.150732>. PMID:27389964.
- Sordi MB, Massochin RC, Camargo AR, Lemos T, Munhoz EA. Oral health assessment for users of marijuana and cocaine/crack substances. *Braz Oral Res.* 2017;31:e102. <http://dx.doi.org/10.1590/1807-3107bor-2017.vol31.0102>. PMID:29267663.
- Souza SJR, Santos AC, Albin MB, et al. Oral health impact profile and associated variables in southern Brazilian drug users. *Iran J Public Health.* 2018;47(10):1466. PMID:30524976.
- Khurshid Z, Zohaib S, Najeeb S, Zafar MS, Rehman R, Ur Rehman I. Advances of proteomic sciences in dentistry. *Int J Mol Sci.* 2016;17(5):728. <http://dx.doi.org/10.3390/ijms17050728>. PMID:27187379.
- Pedersen AML, Sørensen CE, Proctor GB, Carpenter GH, Ekström J. Salivary secretion in health and disease. *J Oral Rehabil.* 2018;45(9):730-46. <http://dx.doi.org/10.1111/joor.12664>. PMID:29878444.
- Chaiben CL, Batista TBD, Penteadó CAS, Barbosa MCM, Ventura TMO, Dionizio A, et al. Salivary proteome analysis of crack cocaine dependents. *Arch Oral Biol.* 2021;121:104952. <http://dx.doi.org/10.1016/j.archoralbio.2020.104952>. PMID:33186792.
- Chaiben CL, Macedo NF, Batista TBD, Penteadó CAS, Ventura TMO, Dionizio A, et al. Salivary protein candidates for biomarkers of oral disorders in people with a crack cocaine use disorder. *J Appl Oral Sci.* 2023;31:e20220480. <http://dx.doi.org/10.1590/1678-7757-2022-0480>. PMID:37194792.
- Drummer OH. Introduction and review of collection techniques and applications of drug testing of oral fluid. *Ther Drug Monit.* 2008;30(2):203-6. PMID:18367981.
- Pil K, Verstraete A. Current developments in drug testing in oral fluid. *Ther Drug Monit.* 2008;30(2):196-202. <http://dx.doi.org/10.1097/FTD.0b013e318167d563>. PMID:18367980.
- Kuwayama K, Miyaguchi H, Yamamuro T, Tsujikawa K, Kanamori T, Iwata YT, et al. Effectiveness of saliva and fingerprints as alternative specimens to urine and blood in forensic drug testing. *Drug Test Anal.* 2016;8(7):644-51. <http://dx.doi.org/10.1002/dta.1831>. PMID:26074137.

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