MAJOR CHALLENGES WHILE ADDITION OF MEDICINAL PLANT MATERIALS IN DENTAL POLYMERS – A CRITICAL ANALYSIS

Anitha Kuttae Viswanathan[1], Rajkumar Krishnan[2], Sabina Mary P[3]

Article History: Received: 12.12.2022 **Revised:** 29.01.2023 **Accepted:** 15.03.2023

Abstract:

Variety of plant parts are used in medical health science owing to its benefits such as anti-inflammatory, anti-infective, antioxidant, antitumorigenic effects. Bioingredients present in it have specific therapeutic potential. Integration of these constituents into dental biomaterials has shown interesting outcome to treat many diseases. In dental material science research, several plant parts are added to achieve superior properties. Till date, there is scarce literature that showed the major challenges while adding the constituents. Definitive remarks regarding its sustainability are yet uncertain. This article discusses on the many difficulties encountered during the incorporation of plant products into denture polymers.

Keywords: Denture Base Resins, Plant Products, Phytochemicals.

[1]Professor, Department of Prosthodontics, SRM dental college, Ramapuram, Chennai, TamilNadu, India.
[2]Dean Academics, Professor & Head, Department of Oral Pathology, SRM dental college, Ramapuram, Chennai, TamilNadu, India.
[3]Postgraduate student, Department of Prosthodontics, SRM dental college, Ramapuram, Chennai, TamilNadu, India.

DOI: 10.31838/ecb/2023.12.s2.015

1. Introduction

Application of dental polymers, started with use of vulcanized rubber, followed by introduction of acrylics, polystyrenes, epoxy resins, polycarbonates, polyethylene, polyether, polyacrylic acids and many more. Wide consumption of polymers is evidenced over the years owing to its basic ability to be molded into desired shape.[1] In dentistry, all specialties utilize dental polymers. It is extensively consumed in prosthodontics, as denture making material, artificial tooth, impression material, implant parts, in provisional restorations, as luting agents, as tooth preparation dies, as radicular retainers, attachment components, as maxillofacial prosthetic material, and in many auxiliary dental equipment as mouth guards, mixing bowls, spatulas.[2]

Amongst the many polymers, methacrylate is widely used in dental prosthetic field owing to its superior physical, mechanical and biological properties. Despite the many advantages, limitations such as inadequate hardness, potential to fracture are observed. Dentures fracture easily when used by geriatric people with loss of fine skills and dexterity.[3] Patients would be unable to wear the denture, if fractured. Efforts are made to improvise its characteristics by addition of newer materials.[4] Various nanofillers of different shapes, sizes, and uses are tried for increasing the fracture strength. Few examples of reinforcing substances researched are organoclay particles, oxides of titanium, aluminum, silica, hydroxyapatite, glass fibers, and many more.[5,6] Another important challenge with PMMA is its surface harboring pathogens leading to denture plaques and biofilm formation. Colonization of microbes on denture surfaces, lead to development of denture stomatitis. When such infections are unattended, it spreads to other systems causing adverse reactions. It is imperative to find out means of prevention of denture infections. [7,8]

Plant parts such as stem, root, leaves, seeds, fruits, flowers, and resins have shown therapeutic benefits against infections. It is used in powder, gels, paste, liquid, and spray forms. Recent preference over synthetic drugs is attributed to its medicinal benefits, minimal side-effects, and usage in drug resistance cases. [9] Propolis was used as topical mucoadhesive gel to treat denture stomatitis by Capistrano HM et al.[10] Vasconcelos LCS et al employed, Punica granatum (pomegranate) as phytotherpeutic gel to limit adherence of microbes in oral cavity.[11] Ethanol extract of Streblus asper Lour leaves showed fungicidal activity against Candida albicans by Taweechaisupapong S et al.[12] In a study done by Hamid SK et al, Azadirachta indica (neem), proved anti-adhesive property in treatment of denture stomatitis.[13] Nair N et al used powdered seeds of Vitis vinifera (Common Grape Vine), in management of candida-associated denture stomatitis.[14] Melaleuca alternifolia (tea tree oil) showed germ tube formation by candida albicans in a study performed by Hammer KA et al.[15]

These are few previous studies where natural products were studied in management of denture infections. Similar to this, enumerable plant herbs are researched to find an optimal one.[16] While performing such research there are many challenges faced by the investigator. Till date, there is scarce studies that have brought these obstacles to limelight. This article, comprehensibly mention the difficulties encountered.

2. Challenges with use of medicinal plants in denture polymers

2.1 Selection of plant species:

World Health organization (WHO) in its 2017 consensus reported 21000 plant species are available for medicinal use. An in-depth search in pharmacopoeia, which contain list of medicinal drugs with their uses and direction of use relative to ethnobotany is important.[17] Understanding categorization by Feeny et al. as “apparent” that includes shrubs and trees and “non-apparent” comprising of herbs is needed. “Apparent” plant species yield organic substances of high molecular weight with less toxicity whereas “non-apparent” ones provide low molecular weight compounds with high toxicity.[18] In health science, more herbs are used because they contain a greater number of bioactive substances than shrubs or trees. Lozano et al., evidenced richness of herbaceous ethnospecies in Cerrado vegetation.[19]

da Silva TC et al., in his study, explained choice between native and exotic plants in alternative medicine therapy. It was described that regional landscape environment, loss of agriculture and transformation into urban culture forced the local inhabitants to opt for exotic plant species for medicinal use.[20] Lail G et al., stated that phytotherapy was used as complimentary to allopathic medicine owing to this reason.[21] A wider therapeutic coverage by exotic than native species was observed by de Medeiros PM et al.[22] Increased palatability, versatility, and nutritional benefits was appreciated with exotic species. According to Cuéllar and Guirado in “Ethnoguided approach” referred to fields of genomics, metabolomics and ecological, botanical taxonomic and epidemiological based studies for choice of plant species.[23] Kantamreddi VS et al., suggested “randomized” approach for plant species selection as there were a greater number of newer bioactive compounds.[24] Guira Cuellar et al., said that in “ecological approach” plants ‘potential biological activities could be used for selection. Otto Richard in 1982 used “Chemosystematic approach” in

selection of particular plant family, genus, species based on specific phytochemicals present in it.[25, 26]
Integration of ethnobotany and medical anthropology is mandatory for therapeutic application in a specific disease. Souza et al in 2004 described significance of ethnopharmacology, wherein biologically active substances were used for health benefit of mankind. Deep literature search aid to identify the curative, prophylactic or diagnostic use of phytochemicals. Social culture of inhabitants, prevalence of particular disease in the locality, access to allopathic medicine, and traditional use of plants in diet for healing purpose signify the role of social sciences in "ethnopharmaceutical" approach. Irrespective of the approach adhered for plant selection, details of its culture or harvest, whether it was grown organically without use of pesticides or chemicals and its botanical identification are very critical factors during selection process.[27]

2.2 Preparation of medicinal plants:
The primary objective involves extraction of appropriate quantity and quality of phytochemical compounds from the plant species. Various solvents such as polar (water, alcohols), intermediate polar (acetone, dichloromethane) and non-polar (hexane, ether, chloroform) are used for this purpose. Techniques including simple maceration, digestion, decoction, infusion, percolation, Soxhlet extraction, ultrasound and microwave assisted extraction can be employed. Procedures of fractionation and purification of extracts are enabled with chromatographic techniques comprising of paper, thin-layer, gas and high-performance liquid chromatographic methods. Once these compounds are obtained, identification process includes use of advanced methodologies such as mass spectroscopy (MS), infrared spectroscopy (IS), ultraviolet spectroscopy (UV), nuclear magnetic resonance spectroscopy (NMR).[28-30]

2.3 Selection of solvent in extraction
Each solvent has its own advantages and limitations. The factors to be considered are 1. Selectivity – the solvent's potential to extract the active ingredient and leave away the inert material. 2. Safety of the solvent to be nontoxic and non-inflammable. 3. Must be cost effective 4. There must not be any reaction between the solvent and the extract 5. The solvent used must be easily recoverable and separable from the extract. 6. Must be viscous enough to permit easy penetration 7. Must not degrade while boiling at high temperature.[31, 32]

2.4 Choice of extraction procedure
The first and foremost element is the stability to heat. Only heat stable plant materials can be extracted with Soxhlet, microwave procedures. Heat labile plants must be extracted with maceration or percolation. Nature of solvent, if its polar then maceration is used, if its volatile percolation and Soxhlet process is used. Financial cost involved in purchase of reagents is important. Duration required for extraction, expected final volume of extract, and its essential intended purpose are other criteria in selection of extraction process.28-32

2.5 Phytochemical screening
This involves, revealing both primary and secondary metabolites in plant extract. Bioactive constituents like phenols, alkaloids, flavonols, flavones, flavonoids, sterols, tannins, proteins, sugars and fats are some examples that are identified. Independent chemical tests are done to determine these substances. Folashade et al., in 2012 stated quality indices based on presence/absence of adulterants, moisture content of extract to gauge its stability, end-volume of crude extract, botanical identification of organic compounds, determination of major classes of compounds, presence/absence of toxic substances. Dragendorff's test, Wagner's test, Mayer's tests are done for alkaloids. Libermann Burchard's test and Salkowski's test for steroids and triterpenoids. Gold Beater's skin test, Gelatin's test for tannins, Shinoda's test, lead acetate test, alkaline reagent test are done for flavonoids. Tests for phenols are ferric chloride test, lead acetate test, and gelatin's test. Biuret's test, ninhydrin test, xanthoproteic tests are done for protein. [33,34]

2.6 Fractionation and purification methods
This separation process is done with either chemical or physical method. With chemical method, suitable reagents like n-hexane, acetone, chloroform and n-butanol are used for segregation. In physical method, its separation based on mass, ion charge, particle size, adsorption potential, and affinity are used.[31, 34]

2.7 Identification method
Recognition of compounds is based on chemical structure and molecular weight by mass spectroscopy. Identification of metabolites with frequency is done with UV method. NMR utilizes number and array of carbon atoms, its arrangement, hydrogen atom and protons. IR method identifies compounds based on its potential to absorb infrared radiation and also determines presence of single, double and multiple bonds. [29,32]

2.8 Storage of plant extract
Once bio-profiling is completed, its stability with same physical, chemical and biological properties until added into dental polymers is a not an easy task. Ideally if it is in powdered form, it is sealed and stored in a vacuum condition. Few extracts loss its properties when exposed to air. For instance corn cob extract powder is stored between 4 to 30 degree Celsius in a microcapsule, is transferred in an

aluminium foil bag and stored in a desiccator. Curcuma ethanol extract lost its antioxidant property when stored beyond 7th day. Storage duration and storage temperature affect the constituents to a significant extent. When stored over long duration, extracts lose their biological activity in it. For expected effect, the extract must be used as soon as feasible for the experiment.[30, 34]

2.9 Addition of plant extract with denture polymers

The purpose of extract addition must always be remembered at every step. Inclusion can influence physical, mechanical and biological properties of the parent polymer. Most commonly used denture polymer is polymethyl methacrylate resin (PMMA). It is available in form of powder (polymer) and liquid (monomer). For polymerization, both polymer and monomer is mixed in ratio of 3:1 either manually or in a amalgamator. The plant extract is added either into polymer powder or into liquid monomer. Form of extract to be added is critical. It must be pre-determined whether powder or liquid form of extract is going to be prepared. Before addition of extract, non-toxic quantity of extract must be identified with performance of anti-microbial tests. Minimum inhibitory concentration tests can be done to find out the lowest concentration of drug required for anti-microbial effect. Monomer volatizes when exposed to air. Incorporation into powder as nanoparticles can be done. Macro sized powder particles become obviously visible while addition. A process called as "Ball-milling" is done to homogenized parent polymer and extract powder. Its duration, revolution per minute (rpm), varies with each type of extract used. Chander N et al performed a 10 minutes ball milling at 300 rpm when chitosan was added into PMMA polymer.[35] Incomplete formation of composite material lead to disproportionate blending and can affect the physical and mechanical properties of the modified biomaterial.

2.10 Choice of polymerization method

Dental PMMA resin can be polymerized using heat-cure, chemical-cure, light-cure, microwave-cure, CAD-CAM and 3-D printing technology. The form of material, time, temperature, equipment involved vary with each method. Influence of plant extract while undergoing specific processing play a vital role. If it evaporates while subjected to high temperatures, the purpose of addition is lost. It must sustain its properties even after retrieval of the processed resin specimen. In conventional heat-cure method, it is processed up to 100 degree Celsius. In chemical cure method, an additional tertiary amine exist for provision of free-radicals in polymerization. Its interaction with additional chemical is questionable fact. CAD-CAM technologies uses subtractive method in form of resin discs. 3D printing layer-by-layer additive technology for processing.[36]

2.11 Effect on properties of extract added dental polymer

Influence of medicinal plant extracts when added into dental polymers is studied under three categories as physical, mechanical and biological properties. Simple incorporation of plant extract must not affect any of these properties. In physical properties, water sorption, solubility, wettability, dimensional stability without alteration in shape or fit due to shrinkage, thermal conductivity to perceive temperature of beverages consumed, colour similar to oral mucosa, texture, colour stability must be retained even after addition of plant extract into polymers. According to ISO 20795-1 sorption and solubility must be less than 32 and 1.6 $\mu g/mm^3$, in order.[37, 38] Mechanical properties such as flexural strength, impact strength, fracture toughness, wear resistance and surface hardness determine the ability of material to withstand tensile, compressive and shear stresses. Fracture toughness describes the ability to withstand crack propagation. Impact strength is the potential to resist denture fracture when high forces are exerted. Based on the ISO 20795-1 guidelines, a minimum of 65MPa is needed with PMMA resins.[39] When any additional material is added into it, there must not be any depreciation in the recommended mechanical values. Biological property is of paramount importance as the modified material needs to sustain in the oral cavity. The polymer has to be biocompatible with no release of toxic elements, devoid of adverse tissue reactions, no cytotoxic effect, must attract less microbes to its surfaces, must allow finishing and polishing of end product, not affect polymerization process.

Formation of biofilms on dental restorative surfaces is a common problem that prevails with any dental material.[40] Functionalization of biomaterials that possess antimicrobial effects is mandatory to prevent occurrence of infections such as dental caries or stomatitis. Addition into polymers as nanoparticles, medicaments and as topical agents are studied. The difficulties encountered are its reliability, effectiveness, sustainability, when used in intraoral conditions.[41, 42]

3. Conclusion

The present article critically analysed the principal challenges faced with use of medicinal plants in dental polymers. Most of the studies done previously are performed in a laboratory set-up and its simulation in live oral conditions may differ. Direct integration of plant material with dental PMMA resin may have a modification of pre-fulfilled properties. Elaborate research must be carried out at experimental conditions before used in-vivo. This domain in research, yet remains challenging and warrants further investigations. Understanding the interaction between two different materials is critical. More clinical studies must be performed only after standardized testing in-vitro platform.

4. References

Zafar MS. Prosthodontic Applications of Polymethyl Methacrylate (PMMA): An Update. Polymers (Basel). 2020;12(10):2299.

Phoenix RD. Denture base materials. Dent Clin North Am. 1996;40(1):113-120.

Al-Dwairi ZN, Tahboub KY, Baba NZ, Goodacre CJ. A Comparison of the Flexural and Impact Strengths and Flexural Modulus of CAD/CAM and Conventional Heat-Cured Polymethyl Methacrylate (PMMA). J Prosthodont. 2020;29(4):341-349.

ShanmugaSundaram, L., Jeyaraj, B. J., Krishnan, M., & Balasubramanian, M. (2021). Evaluation of Bond Strength on Surface Treated Denture Teeth to Injection Molded PMMA Denture Base. Annals of Dental Specialty, 9(1), 7-12

Tah R, Chidambaranathan AS, Balasubramanium MK, Sundaram SM. Effect of Zirconia Silica Nanofibers on Flexural Strength of Feldspathic Ceramic - An Experimental Study. Adv Biomed Res. 2021;10:31.

Chander NG, Jayaraman V. Estimation of IZOD impact strength between different concentrations of chitosan-reinforced denture base resins. Indian J Dent Res. 2021;32(3):380-384.

Raszewski Z, Nowakowska-Toporowska A, Nowakowska D, Więckiewicz W. Update on Acrylic Resins Used in Dentistry. Mini Rev Med Chem. 2021;21(15):2130-2137.

Gad MM, Fouda SM, Al-Harbi FA, Näpänkangas R, Raustia A. PMMA denture base material enhancement: a review of fiber, filler, and nanofiller addition. Int J Nanomedicine. 2017;12:3801-3812. Published 2017 May 17.

Anitha KV, K R. Management of Denture Infection with Phytomedicine [published online ahead of print, 2022 Aug 29]. Infect Disord Drug Targets. 2023; 23(2): 13-20.

Capistrano HM, de Assis EM, Leal RM, Alvarez-Leite ME, Brener S, Bastos EM. Brazilian green propolis compared to miconazole gel in the treatment of Candida-associated denture stomatitis. Evid Based Complement Alternat Med. 2013;2013:947980.

Vasconcelos LC, Sampaio MC, Sampaio FC, Higino JS. Use of Punica granatum as an antifungal agent against candidosis associated with denture stomatitis. Mycoses. 2003;46(5-6):192-196.

Taweechaisupapong S, Klanrit P, Singhara S, Pitiphat W, Wongkham S. Inhibitory effect of Streblus asper leaf-extract on adhesion of Candida albicans to denture acrylic. J Ethnopharmacol. 2006;106(3):414-417.

Hamid SK, AlDubayan AH, Alghamdi LA, et al. Mechanical, Surface, and Optical Properties of PMMA Denture Base Material Modified with Azadirachta indica as an Antifungal Agent. J Contemp Dent Pract. 2021;22(6):655-664.

Nair N, Mahajan S, Chawda R, Kandaswami C, Shanahan TC, Schwartz SA. Grape seed extract activates Th1 cells in vitro. Clin Diagn Lab Immunol. 2002;9(2):470-476.

Hammer KA, Carson CF, Riley TV. Melaleuca alternifolia (tea tree) oil inhibits germ tube formation by Candida albicans. Med Mycol. 2000;38(5):355-362.

Casaroto AR, Lara VS. Phytomedicines for Candida-associated denture stomatitis. Fitoterapia. 2010;81(5):323-328.

de Albuquerque UP. Re-examining hypotheses concerning the use and knowledge of medicinal plants: a study in the Caatinga vegetation of NE Brazil. J Ethnobiol Ethnomed. 2006;2:30.

Feeny p. "Plant apparency and chemical defense," in Biological Interactions Between Plants and Insects: Recent Advances in Phytochemistry, J. W. Wallace and R. L. Nansel, Eds., Plenum Press, New York, NY, USA, 1976.

Lozano A, Araújo EL, Medeiros MF, Albuquerque UP. The apparency hypothesis applied to a local pharmacopoeia in the Brazilian northeast. J Ethnobiol Ethnomed. 2014;10:2. Published 2014 Jan 10.

da Silva TC, da Silva JM, Ramos MA. What Factors Guide the Selection of Medicinal Plants in a Local Pharmacopoeia? A Case Study in a Rural Community from a Historically Transformed Atlantic Forest Landscape. Evid Based Complement Alternat Med. 2018;2018:2519212.

Lail G, Luck N, Tasneem AA, Rai A, Laeeq SM, Majid Z. The usage of complementary and alternative medicine in gastrointestinal patients visiting the outpatients' department of a large tertiary care centre-views from Pakistan. Pan Afr Med J. 2016;24:247.

de Medeiros PM, Ladio AH, Albuquerque UP. Patterns of medicinal plant use by inhabitants of Brazilian urban and rural areas: a macroscale investigation based on available literature. J Ethnopharmacol. 2013;150(2):729-746.

Tirloni CAS, Palozi RAC, Schaedler MI, et al. Biomonitoring the cardiorenal effects of Luehea divaricata Mart.: An ethnoguided approach. J Ethnopharmacol. 2018;225:53-63.

Kantamreddi VS, Wright CW. Screening Indian plant species for antiplasmodial properties--ethnopharmacological compared with random selection. Phytother Res. 2012;26(12):1793-1799.

Heinrich M. Ethnobotany and its role in drug development. Phytother Res. 2000;14(7):479-488.

Heinrich M. Ethnobotany and natural products: the search for new molecules, new treatments of old diseases or a better understanding of indigenous cultures?. Curr Top Med Chem. 2003;3(2):141-154.

Suárez ME. Medicines in the forest: Ethnobotany of wild medicinal plants in the pharmacopeia of the Wichí people of Salta province (Argentina). J Ethnopharmacol. 2019;231:525-544.

Ingle KP, Deshmukh AG, Padole DA, Dudhare MS, Moharil MP, Khelurkar VC. Phytochemicals: Extraction methods, identification, and detection of bioactive compounds from plant extracts. J Pharmacogn Phytochem. 2017;6:32–6

Azwanida NN. A review on the extraction methods use in medicinal plants, principle, strength, and limitation. Med Aromat Plants. 2015;4:196.

Pandey A, Tripathi S. Concept of standardization, extraction, and pre-phytochemical screening strategies for herbal drug. J Pharmacogn Phytochem. 2014;2:115–9.

Sasidharan S, Chen Y, Saravanan D, Sundram KM, Yoga Latha L. Extraction, isolation and characterization of bioactive compounds from plants' extracts. Afr J Tradit Complement Altern Med. 2011;8:1–10.

Altemimi A, Lakhssassi N, Baharlouei A, Watson DG, Lightfoot DA. Phytochemicals: Extraction, isolation, and identification of bioactive compounds from plant extracts. Plants. 2017;6:42.

Abubakar AR, Haque M. Preparation of Medicinal Plants: Basic Extraction and Fractionation Procedures for Experimental Purposes. J Pharm Bioallied Sci. 2020;12(1):1-10.

Ong ES, Cheong JS, Goh D. Pressurized hot water extraction of bioactive or marker compounds in botanicals and medicinal plant materials. J Chromatogr A. 2006;1112(1-2):92-102.

Chander NG, Venkatraman J. Mechanical properties and surface roughness of chitosan reinforced heat polymerized denture base resin. J Prosthodont Res. 2022;66(1):101-108.

Prpić V, Schauperl Z, Ćatić A, Dulčić N, Čimić S. Comparison of Mechanical Properties of 3D-Printed, CAD/CAM, and Conventional Denture Base Materials. J Prosthodont. 2020;29(6):524-528.

Alqahtani M. Mechanical properties enhancement of self-cured PMMA reinforced with zirconia and boron nitride nanopowders for high-performance dental materials. J Mech Behav Biomed Mater. 2020;110:103937.

Ali IL, Yunus N, Abu-Hassan MI. Hardness, flexural strength, and flexural modulus comparisons of three differently cured denture base systems. J Prosthodont. 2008;17(7):545-549.

de Oliveira Limírio JPJ, Gomes JML, Alves Rezende MCR, Lemos CAA, Rosa CDDRD, Pellizzer EP. Mechanical properties of polymethyl methacrylate as a denture base: Conventional versus CAD-CAM resin - A systematic review and meta-analysis of in vitro studies. J Prosthet Dent. 2022;128(6):1221-1229.

Freitas RFCP, Duarte S, Feitosa S, et al. Physical, Mechanical, and Anti-Biofilm Formation Properties of CAD-CAM Milled or 3D Printed Denture Base Resins: In Vitro Analysis [published online ahead of print, 2022 Jun 4]. J Prosthodont. 2022;10.1111/jopr.13554.

Khattar A, Alghafli JA, Muheef MA, et al. Antibiofilm Activity of 3D-Printed Nanocomposite Resin: Impact of ZrO_2Nanoparticles. Nanomaterials (Basel). 2023;13(3):591. Published 2023 Feb 1.

Thanigaivel, S., Vickram, S., Dey, N., Gulothungan, G., Subbaiya, R., Govarthanan, M., ... & Kim, W. (2022). The urge of algal biomass-based fuels for environmental sustainability against a steady tide of biofuel conflict analysis: Is third-generation algal biorefinery a boon?. Fuel, 317, 123494.

Kettel MJ, Heine E, Schaefer K, Moeller M. Chlorhexidine Loaded Cyclodextrin Containing PMMA Nanogels as Antimicrobial Coating and Delivery Systems. Macromol Biosci. 2017;17(2):10.1002/mabi.201600230.