e-ISSN: 2637-0611

Available online at
https://myjms.mohe.gov.my/index.php/corals

Compendium of Oral Science 11(2) 2024, 96 – 112

**Compendium of Oral Science**

# Investigation on the Impact of Bisphenol A Exposure from Dental Materials: A Systematic Review

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ARTICLE INFO

*Article history:*
Received 12 May 2023
Revised 22 August 2023
Accepted 25 November 2023
Online first
Published 1st September 2024

*Keywords:*
bisphenol A
dental material
human health
adverse effect
free-BPA materials

*DOI:*
10.24191/cos.v11i2.27506

ABSTRACT

Bisphenol A (BPA) has been reported to have many impacts on human health due to its excessive exposure in human daily life. This includes patients that received dental treatment as they may be exposed to dental materials containing BPA. Few studies discuss the alternatives to replace BPA to reduce its exposure to humans as well as clinical practice prevention to reduce BPA leaching retained in the oral cavity. Thus, the aim of the study is to systematically review the impact of BPA exposure from dental materials on human health and to provide suggestions on the substitution of BPA with other materials or free-BPA materials. This study was performed through PubMed, ScienceDirect, and Scopus databases. The data were extracted by all authors independently and tabulated according to the topic, author, impact of BPA on human health, suggestion on substitution of BPA with other materials or free BPA materials, and limitation of the studies. About fifty-eight studies related to BPA usage in dental treatment, short- and long-term exposure of BPA, and health risk exposure to BPA were shortlisted. Almost all studies reported that BPA exposure from dental material showed negligible dosage that may not harm human health. However, there is a clear indication showing a small amount of BPA leaching from dental materials in the short term after application. About fifteen papers suggested an approach to minimize the usage of BPA materials including the introduction of free-BPA materials such as G- IEMA, ISBGBMA, TTM monomer, FDMA monomer, BCF-GMA, PCDMA and TMBPF- Ac, and prevention in clinical practice. In conclusion, BPA is known to affect human health but there is a low risk when related to BPA exposure from dental materials. However, it should not be neglected due to the lack of studies on long-term effects that may create a possible risk to human health. Therefore, suggestions on free-BPA material should be considered to reduce the exposure of BPA in humans.

## INTRODUCTION

Bisphenol A (BPA) is a synthetic chemical that is used to make epoxy resins and polycarbonate plastics, which can be found in various products like food packaging and pesticides. Recently, BPA has been reported to potentially cause severe biological effects because of its abundant environmental usage (Sabour

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et al, 2021). BPA has been linked to the pathogenesis of many endocrine disorders, including female and male infertility, precocious puberty, hormone-dependent tumors such as breast and prostate cancer, and neuroendocrine system disorders, leading to abnormal nervous system development through a variety of routes of contamination, including the respiratory, digestive, and cutaneous tract (Kloukos et al, 2013; Sabour et al, 2021). For the majority of the studied subgroups, the exposure to BPA from non-food sources such as exposure through dust, thermal paper, dental materials, and medical devices is typically at least one order of magnitude lower than the exposure from food sources (Geens et al, 2012).

BPA is also a precursor to (bis-GMA) Bisphenol-A-glycidyl methacrylate, which is the principal monomer used in composite resins (Sabour et al, 2021). Currently, composite is widely used because of its characteristics that display good mechanical and physical and the significant potential to generate additional functionality such as antibacterial and therapeutic activities (Sabour et al, 2021). These dental resin composites (DRCs) have been gradually extended for direct restoration on the anterior and posterior teeth (Sabour et al, 2021).

Furthermore, BPA has gotten much attention in the orthodontic industry in recent years (Halimi et al, 2016). As a precursor of bisphenol A-glycidyl methacrylate (bis-GMA) and bisphenol A dimethacrylate (bis-DMA), BPA is used to manufacture the monomers found in orthodontic composites. BPA is also used to make the polycarbonate matrix that many plastic brackets and orthodontic splints are made of. Brackets and other orthodontic accessories are bonded to tooth surfaces using bis-GMA-based composite materials (Halimi et al, 2016). For the past 40 years, composite resins have been utilized successfully for bracket bonding in orthodontics. These polymer applications in orthodontic material applications have brought new levels of creativity, practicality, and aesthetics to the field (Kloukos et al, 2013). In addition, the amount of BPA leaking from the Bis-GMA–based resin composite used to bond orthodontic lingual retainers was low, and far below daily intake reference doses. However, there is some evidence of a "low-dose effect," the amount of BPA released from resin composites used in lingual bonded retainers should not be ignored (Kang et al, 2011). The immediate release of BPA appears to come mainly from the resin's uncured layer (Kang et al, 2011).

Newborn children's metabolic processes are not sufficiently developed (Chung et al, 2012). They are more susceptible than adults to the negative consequences of similar levels which are below the tolerable daily intake of external BPA exposure. Therefore, it is crucial to determine BPA levels obtained from resin composite exposure in children. In addition, a study has been conducted that revealed the significant BPA levels in the children's bodies as a result of resin-based dental products (Chung et al, 2012) Breast milk and polycarbonate feeding bottles are the predominant sources of BPA exposure among infants, while oral exposure from canned foods becomes the primary source of BPA exposure as children age (Kloukos et al, 2013).

Based on the United States Environmental Protection Agency studies, the reference dose for BPA is 50 µg/kg bw/day. However, the European Food Safety Authority (EFSA) reduced the tolerable daily intake (TDI) from 50 µg/kg bw/day in 2015 to 4 µg/kg bw/day in response to a refined risk assessment of BPA and its unfavorable health consequences (EFSA, 2015). According to the EFSA, average BPA exposure levels from food are well below the TDI, and BPA does not create a health concern to any population, including unborn children, infants, and children. However, as a result of the extensive and inevitable exposure to humans, rising concerns about BPA use prompted numerous countries to impose restrictions on BPA use, resulting in manufacturers abandoning the use of BPA (Ma et al, 2019).

Therefore, the justification of this research is to provide a new collection of data on the impact of BPA related to dental materials and alternatives to BPA since there is limited information regarding this concern. Hence, our study aims to investigate the impact of Bisphenol A exposure from dental materials on human health and to provide suggestions on the substitution of BPA with other materials or free-BPA materials.

https://doi.org/10.24191/cos.v11i2.27506 

## MATERIALS AND METHOD

### Literature search strategy

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The search for published articles was performed through three electronic databases which are PubMed, ScienceDirect and Scopus. The Boolean search involved the combined use of the terms such as “BPA”, “dental material”, “impact”, “adverse effect”, “risk”, “BPA in dental material”, “leaching of BPA from dental material” and “impact of BPA on human health”. The filter used is the publication date from 1/1/2011 to 1/12/2022.

### Study selection

According to PICO which stands for population, intervention, comparison and outcome, our targeted population was patients who received dental treatment, including adults, children, pregnant women, or individuals aged between 6-65 years old. Patients who received dental treatment are more likely exposed to dental materials that contain BPA as our intervention in this study and we compare the intervention with the substitution of free-BPA materials usage for dental treatment. The outcome of this study is to investigate the impact on human health due to BPA exposure from dental materials.

The inclusion criteria of this systematic review included (a) studies between 2011 to 2022, (b) primary and secondary research studies, (c) individuals aged between 6-65 years old including pregnant women and (d) in vitro or in vivo studies. The exclusion criteria included (a) non-English articles, (b) literature review, (c) outdated studies and (d) individuals with poor general health.

### Data extraction

Based on the PRISMA diagram 2020 guideline, the number of articles screened via databases and other methods were counted (n=) and duplications were removed using the Mendeley application. The titles and abstract were screened based on predefined criteria and excluded. Full text of remaining articles was reviewed and screened for eligibility of inclusion and exclusion criteria. Studies that meet the inclusion criteria were recorded and reviewed in this study. As for data tabulation, Microsoft Excel was used to tabulate our findings according to the year, topic, author, significance of the investigated topic, and limitation of the studies.

The significance of the investigated topic is further divided into common dental material that release bisphenol A, effect of BPA on short- and long-term exposure that release from dental material, impact of BPA release from dental materials on the body human system and how to minimize BPA exposure from dental materials. The papers were counted, reviewed, and discussed by section which are a) bisphenol A usage in dental treatment, b) short- and long-term exposure of BPA, c) health risk of exposure to BPA and d) approach to minimize BPA exposure.

## RESULTS

By using the keywords and filtered search, 47 articles were recorded from PubMed, 13 articles from ScienceDirect and 138 articles from Scopus databases. All the access articles were transferred into Mendeley, and 59 duplicate records were removed. 139 articles were screened based on titles and abstract based on predefined criteria. 60 articles were excluded, and 79 articles were assessed for eligibility criteria. 21 articles were excluded due to a) individual with poor general health (n=1), b) review free-BPA materials (n= 2), c) not discussed BPA released from dental materials (n=6), d) commentary articles (n=2) and e) not really discussed adverse effect of BPA (n=10). Other relevant references were identified and obtained from

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5 websites and 1 e-book. In total, 58 studies that met the inclusion criteria will be reviewed and discussed in this paper. (Figure 1).

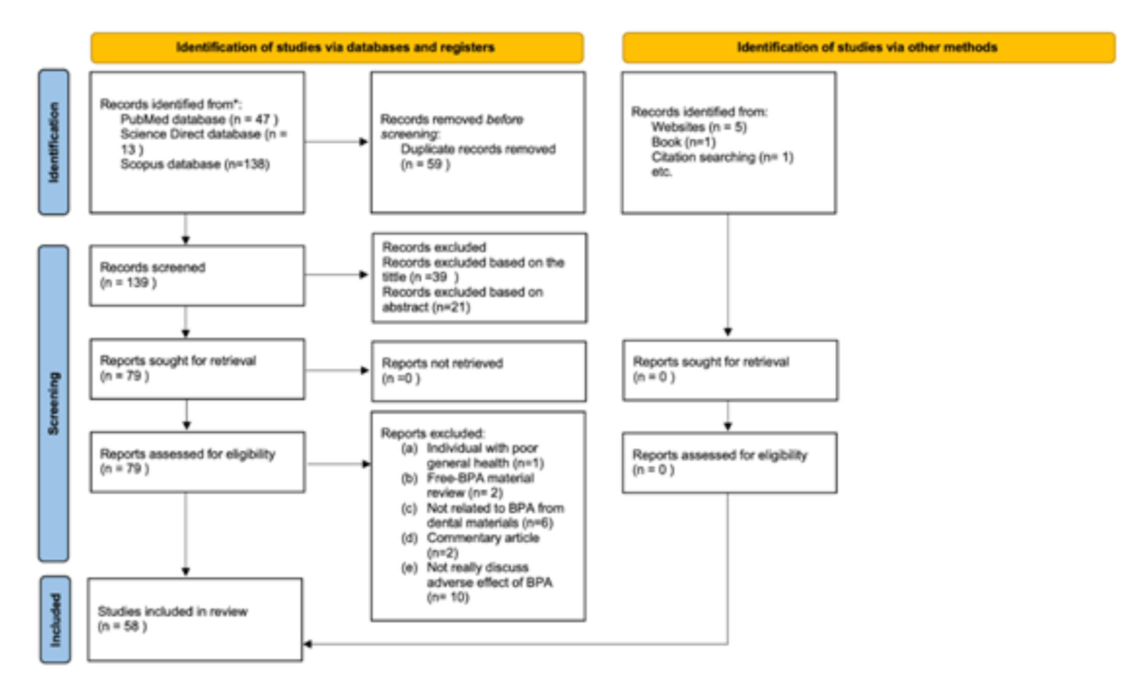


Fig. 1. PRISMA flowchart of the literature selection process of the present systematic review

19 papers had discussed the usage of BPA in dental treatment, and it found out that the most common materials containing BPA are orthodontic adhesive, fissure sealant, and resin-based composite. These materials containing BPA are known to leach from dental materials into the oral cavity in which 12 papers regarding short- and long-term BPA exposure had discussed in this paper to address the concern of timing and effect of this chemical retained in the mouth. 13 articles were highlighted to address the issue regarding the impact of BPA from dental materials on the human body system such as endocrine system, reproductive system, central nervous system, and respiratory system. 15 studies identified proposed approaches to minimize BPA exposure such as the introduction of free-BPA materials and clinical prevention to reduce BPA exposure during dental treatment.

To the best of our knowledge, this is the updated paper that reviewed the latest research regarding BPA exposure from dental materials and all other additional searches related to it within the timeframe of 12 years of study from 2011 to 2022 to benefit all dental practitioners and the communities in dentistry. Most importantly, dental practitioners will also be able to concede, or reconsider choosing the best dental materials due to dental treatment and take a step ahead of precaution when dealing with these BPA-containing materials. In addition, a collection of discussions, suggestions, alternatives, and limitations from current findings and different studies will also be reviewed in this paper to maximize the knowledge of BPA exposure from dental materials among health practitioners worldwide.

https://doi.org/10.24191/cos.v11i2.27506 

## DISCUSSION

### Bisphenol a usage in dental treatment

#### 1. Orthodontic adhesive

There are three papers studied about the release of BPA from orthodontic usage. Different materials are needed for both removable and fixed appliances in orthodontic treatment. Orthodontic appliances can remain in the mouth cavity for a short while to several years, during which time environmental factors can alter the materials' biodegradability and durability. It is more important when using fixed lingual retainers since the composite resin is in contact with the oral cavity for a longer period than bracket bonding adhesives. After a month, a light-cured bracket adhesive used to bond lingual fixed retainer's releases BPA in vitro. As the composite resin is exposed to the oral cavity for a longer period than a bracket bonding adhesive, using fixed lingual retainers makes this issue much more important (Sifakakis & Eliades, 2017).

Although previous research has shown that the amounts of BPA produced by this kind of dental material are below the no-observed-adverse-effect level and lowest-observed-adverse-effect level (NOAEL/LOAEL) limit, these low doses are still thought to be an additional source of exposure and may have negative effects. Similar to past research done with orthodontic materials, BPA levels in the urine of the participants in the present investigation were quite low and much below-specified limits (Horta et al, 2018). BPA was discovered to leach from thermoformed Biocryl acrylic resin retainer material and a completely cured Transbond XT orthodontic adhesive during 3 days of artificial saliva immersion under the rigorous mechanical and thermal conditions of the investigation (Kotyk & Wiltshire, 2014). Although the levels of leached BPA were below the recommended daily intake, prior research indicates that patient BPA exposure should be reduced and perhaps even eliminated (Kotyk & Wiltshire, 2014).

The composite resin used to bond fixed appliances has less exposure to BPA than lingual bonded and acrylic resin retainers because the retainer will be used for life. The more they use retainers the more they will be exposed to the BPA. Retainers are important to make sure their teeth are not shifting back to their original position after de-bond fixed appliances. However, the study proved that it is still below the no observed adverse effect level (NOAEL)/ low observed adverse effect level (LOAEL) limit but can be worsened if a human were exposed to BPA other than dental materials sources such as food packaging that is also widely used.

#### 2. Fissure sealant

There are eight papers that studied the leaching of BPA from one of the commonly used dental materials which is fissure sealant. Fissure sealant is a material that is placed in the pits and fissures to prevent or control dental caries development (Ministry of Health Malaysia, 2020). There are two types of materials that are commonly used: resin-based, the first choice of treatment, or glass ionomer sealants as a provisional agent when absolute isolation is uncompromised (Sreedevi et al, 2021). It is known that fissure sealant containing BPA may leach immediately after application and is likely to be from hydrolysis of a common monomer used in dental resin formulation which is bisphenol A Dimethacrylate, Bis-DMA (Rathi et al, 2012).

However, the amount of monomer is very low as no significant BPA has been detected in blood samples indicating no systemic exposure of BPA from dental sealant (Rathee et al, 2012). A study by The New England Children's Amalgam Trial (NECAT) which investigated the relationship between dental sealant exposure to psychosocial and other health outcomes of children aged six to ten years old over the course of five-year follow-up shows that cumulative exposure to sealant was not linked to behavioral, neuropsychological, or physical development (body composition/body mass index) in children (Maserejian et al, 2014).

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There is also no statistically significant association between the number of sealants/restoration and urinary BPA concentrations in a nationally representative sample of U.S. children (McKinney et al, 2014). In research conducted among Korean children in 2012, BPA from dental sealant/resin was detected in saliva after placement due to bis-DMA hydrolysis by salivary esterases (Han et al, 2012). However, the detectable doses of BPA in saliva are below the tolerable daily intake level of BPA, which is 50 µg per kilogram per day based on the United States and the European Food Safety Authority (EFSA) (USEPA, 2023; EFSA, 2010).

Fissure sealant is usually used in patients with early caries lesions with deep fissures to prevent and control further caries formation. The study has been done by investigating the urine and blood samples of patients that have fissure sealants on their teeth. Even though there is high leaching of BPA after immediate application of the dental material, it is still below the tolerable daily intake based on EFSA.

### 3. Resin-based composite

There are eight papers that studied the effect of BPA release from resin-based composite. The most widely used dental materials are composites and sealants made of bis-GMA (bisphenol A-glycidyl methacrylate). Over 28 million children have dental sealants, and nearly 30 million children have dental restorations. BPA derivatives are used in more than 85% of composites. Nearly two-thirds of sealants contain Bis-GMA, whereas just 15% of dental composites do not. The use of BPA in the production of dental products is discouraged by the World Dental Federation. However, because it offers vital physical qualities (stiffness, hardness) that guarantee lifetime, bisGMA is frequently used in dental materials. Due to its widespread use, dental procedures are frequently a source of BPA exposure for the general population. However, it is unclear how dental-related BPA exposure may affect a person's health (McKinney et al, 2020).

The degree of polymerization of composite resins can be negatively impacted by improper curing conditions, which can also lead to a decline in the resin's characteristics. As a result, there would be a rise in the release of unreacted monomers, which can be harmful to cells (Kwon et al, 2015). In studies on human gingival fibroblast, light-cured composite resins (Clearfil ES-2, Clearfil ES Flow, Filtek Supreme XTE, Grengloo, Blugloo, Transbond XT, and Transbond LR) release components such as BPA and TEGDMA which are slightly cytotoxic to this cell (Bationo et al, 2021). Another study state that the 3M ESPE dental composite restoratives, dental sealants, and orthodontic adhesive products examined in this study may expose people to very low levels of BPA, but they do not exceed the BPA safety criteria currently in place, thus there is no risk to the patient (Bagley et al, 2021). The release of BPA increased as curing time increased or as the curing distance decreased. Contrary to TEGDMA and UDMA studies, increased monomer release was generally caused by longer curing distances and shorter curing times. The results of this study indicated that based on the main components and component ratios of commercial composite resins, different curing durations and distances are advised (Kwon et al, 2015).

The degradation of the composite, on the other hand, can leak monomers from CAD/CAM resin-based dental materials into the oral cavity. The identification of leaking monomers is crucial because, especially in high quantities, these substances may seriously harm humans if they enter the body. The vast majority of resin-composite CAD/CAM material manufacturers do not specify the precise composition of their product in the material safety data sheet. The chosen materials for this study's materials were accurately identified by their compounds, including their names and CAS numbers for each methacrylate (Diamantopoulou et al, 2020).

One hour after the placement of the restoration, there were noticeable increases in salivary concentrations of BPA and other research components, and nine to thirty hours later, there was an increase in the concentration of BPA in urine (Kingman et al, 2012; Tichy et al, 2022). The study found that using rubber dams had no impact on the amount of BPA that was being absorbed and excreted in the urine

https://doi.org/10.24191/cos.v11i2.27506 

(Kingman et al, 2012). There is another study stated that immediately following the placement of the dental polymer-based restorations, there was a statistically significant rise in salivary BPA levels. After placement, the levels of BPA gradually and rapidly reduced. The salivary BPA level was only slightly higher a week after treatment compared to before treatment. After therapy, there was no statistically significant difference in the BPA content in the urine (Berge et al, 2019).

Nowadays, resin-based composites are widely used in dentistry because of aesthetics and their good mechanical and biological properties to the tooth such as wear resistance, toughness, hardness, anti-microbial, and remineralization effects. There are a few factors that influence the release of BPA from the product such as the distance of light cure, the time taken of the light cure, and the usage of the rubber dam during the restoration procedure. However, the BPA release from those dental material products alone does not exceed the BPA safety criteria.

## 4. Short- and long-term of BPA

Twelve articles were identified and obtained to rule out the effect of short- and long-term BPA exposure to human health. Since BPA is widely used in daily life, humans may be exposed to this substance in many routes such as oral, by inhalation or transdermal (Konieczna et al, 2015). In a clinical dental setting, dental material is one of the main sources of BPA, which is often leached into the oral cavity (Drozdz et al, 2011). Recently, partial salivary and bacterial degradation of monomers such as bis-GMA, bis-EMA, bis-PMA, and BADGE was found to increase the BPA levels in saliva but only <1% are present within 48 hours, which is irrespective of the amount of BPA in material (De Nys et al, 2021a).

Children and adolescents who receive bis-GMA-based restorations may experience transient elevations in urinary BPA levels that subside in urine samples given 14 or 6 months following the treatment. Due to the wide range of background BPA exposure, changes in urine BPA concentrations following the placement of a few restorations might not be noticeable. According to these findings, BPA leaching from recently placed composite restorations ceases being detectable in urine two weeks after placement. Such short-term exposure may be unclear on human health (Maserejian et al, 2016).

Another finding may conclude that BPA exposure is brief and sporadic as the largest amounts are only found in saliva immediately following or an hour after placement (Kloukos et al, 2013). BPA was not discovered in saliva at levels above 0.21 ng/ml, which is known to be the geometric mean of the BPA baseline, showing that the exposure of BPA from dental materials was brief and did not retain in saliva in measurable amounts beyond 60 minutes (Becher et al, 2018). Other studies also stated that through the application of lingual orthodontic retainers with resin-matrix composites on patients, salivary BPA levels of about 2.09x10-2 g/ml were discovered. The absorption into oral and gastrointestinal mucosa will increase if there is an increased release of BPA which will lead to increased risks of getting local and systemic toxicity (Lopes-Rocha et al, 2021).

To study the long-term effect of BPA elution, (De Nys et al, 2021b) had concluded that resin-based composites continue to release in water and ethanol over 1 year in vitro. However, no evidence has been reported of long-term effects in vivo as saliva contains proteins and enzymes with esterase activity compared to ethanol as an organic solvent. BPA may be assessed in large epidemiological studies using ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) method to analyse BPA release in saliva and urine in vivo over a longer period (De Nys et al, 2018). Moreover, the study agreed there might be a possible associated health effect when it comes to human exposure to BPA from dental material; thus, more research is necessary.

The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) stated that long-term oral exposure to BPA via dental materials poses a negligible risk to human health (Berge et al, 2019). The European Food Safety Authority (EFSA) also concluded that it is unlikely that the general

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population is chronically exposed to BPA from dental materials and thus it was not further considered in the EFSA exposure calculations (EFSA, 2015). In 2017, American Dental Association (ADA) Council on Scientific Affairs stated, “The ADA supports ongoing research on the safety of existing dental materials and in the development of new materials. Based on current research, the Association agrees with the authoritative government agencies that the low level of BPA exposure that may result from dental sealants and composites poses no known health threat” (American Dental Association, 2023). Therefore, it can be concluded that BPA arising from dental materials is not a chronic exposure and does not pose a threat to human health in a short- and long-term effect.

**Health risk of exposure to BPA**

**1. Impact of BPA on endocrine system**

There are four articles that were nicely recognized to explain about the BPA exposure that affects the human endocrine system. The endocrine system is a group of glands without ducts that create and release hormones into the circulatory system. To transport secretions to their targeted organs, endocrine glands function without ducts. Contrarily, hormones have the ability to communicate chemically with a variety of cells and tissues at once. BPA, which has the capacity to interfere with naturally occurring hormones in the human body serum and is known to interfere with endocrine function by mimicking oestrogen, Increased androgen concentrations are highly correlated with higher BPA levels. The pituitary glands oestrogen receptors are directly contacted by BPAs, which prevents the pituitary gland from secreting follicle-stimulating hormone (FSH) (Chung et al, 2012). Although the prolactin cell population was unaffected after dental fillings, small amounts of BPA eluted during mastication can affect immunocytochemical patterns of pituitary cells, increasing cellular proliferation in the short, medium, and long terms (Velasco-Marinero et al, 2011).

Human exposure to this chemical can occur orally, inhaled, or transdermally, among other ways (Konieczna et al, 2015). BPA has been demonstrated to interact with oestrogen receptors and to operate as an agonist or antagonist through signalling pathways that are dependent on the oestrogen receptor (ER). This is because of its phenolic structure. Therefore, it has been demonstrated that BPA contributes to the pathogenesis of a number of endocrine disorders, such as male and female infertility, early puberty, hormone-dependent tumours including breast and prostate cancer, and a variety of metabolic disorders like polycystic ovary syndrome (PCOS).

BPA seems to need specific considerations, such as biomonitoring, due to the persistent, daily exposure and tendency to bioaccumulate. This observation should include clinical testing to measure the amount of BPA in the urine, as this is not only one of the best ways to assess exposure to this substance, but also a way to determine the relationship between daily BPA consumption and the risk of developing certain endocrine disorders (Konieczna et al, 2015).

Precocious puberty may also be caused by BPA exposure, according to data from animal studies. In comparison to the control group, prenatal rats exposed to BPA doses of 2 mg/kg body weight per day experienced an acceleration of puberty. It seems that exposure to BPA causes precocious puberty mostly resulting from weak estrogenic action, which via a positive feedback loop stimulates the activity of the GnRH pulse generator, increasing the secretion of LH and FSH by the pituitary. Studies on males with prostate cancer revealed that their urine had substantially greater levels of BPA than that of the control group. Polycystic ovarian syndrome (PCOS), the most prevalent endocrinopathy in women of childbearing age, may also be affected. BPA blood concentrations were substantially greater in PCOS patients—particularly obese ones—than in healthy controls (Konieczna et al, 2015).

PCOS aetiology is complex. One of the hypothesised mechanisms by which BPA may contribute to the pathogenesis of this syndrome is the activation of the hypothalamic GnRH pulse generator, which

https://doi.org/10.24191/cos.v11i2.27506

results in a steady rise in plasma LH concentrations and, in turn, stimulates the production of androgen in the ovaries and interferes with the proper development of ovarian follicles (Konieczna et al, 2015).

### 2. Impact of BPA on the reproductive system

Four articles were used to explain the effect of BPA on the reproductive system. The biological system composed of all the anatomical parts involved in sexual reproduction is the reproductive system of an organism, commonly referred to as the genital system. According to the Endocrine Society, endocrine-disrupting chemicals (EDCs) are substances in the environment such as BPA that interfere with the normal function of the body's endocrine system and act like “hormone mimics” because they may alter many hormones including reproductive hormones (Endocrine Society, 2023). BPA causes effects by a variety of pathways, the majority of which include binding to oestrogen receptors (ER) and interacting with nuclear receptors, causing changes in metabolism, hormone function, or epigenetic dysregulation, benign alterations in human ovaries, including endometriosis, cystic endometrial hyperplasia, ovarian cysts, and the progressive growth of the oviducts and development of ovarian cancer (Dumitrascu et al, 2020).

Meanwhile, males are shown to be more affected than females by phthalates, a group of chemicals used to make plastic more durable which have been discovered to have antiandrogenic effects (Solleiro-Villavicencio et al, 2020). In laboratory animals, BPA has been found to have very low acute oral toxicity, with LD50 values greater than 2000 mg/kg of body weight, concluding that BPA exposure from dental resins was determined to have no negative effects on reproduction at 0.05 mg/kg body weight/day dosages, which is lower than the reference dose (Rathee et al, 2012).

### 3. Impact of BPA on the central nervous and respiratory system

There are a few articles studied about the effect of BPA exposure to the central nervous and respiratory system. The respiratory system is a biological system made up of organs and structures that are employed for gas exchange. The findings of this study may provide insight into the rising prevalence of respiratory conditions among dental professionals, and extra precautions should be taken to avoid inhaling composite dust. Small amounts of BPA, an endocrine disruptor that can accidentally probably end up in composites as a by-product of the manufacturing of certain methacrylate monomers, were also released by all composite dust particles (Cokic et al, 2017).

The part of the nervous system that is made up mostly of the brain and spinal cord is known as the central nervous system (CNS). Studies investigating the impact of BPA on living organisms have demonstrated its negative effects on laboratory animals' reproductive systems and supported the theory that pregnant women exposed to this substance may experience foetal birth defects, damage to the nervous system, and behavioural changes in their offspring. In an experiment by (Salian et al, 2009) decreased spermatogenesis in newborn male rats and an increased propensity for miscarriage in newborn female rats were used to show how prenatal exposure to BPA affects the ability of subsequent generations of animals to reproduce (Malkiewicz et al, 2015).

Even at dosages below the current NOAEL, no-observed-adverse-effect level, prenatal BPA exposure may also alter the expression of the estrogen receptor and oxytocin genes in the developing brain (Arambula et al, 2016). There is also no association between the placement of polymer-based fillings during pregnancy and adverse birth outcomes (Berge et al, 2018).

https://doi.org/10.24191/cos.v11i2.27506 

**Approach to minimize BPA exposure**

Based on our findings, about fifteen papers proposed their approach to minimize BPA exposure from dental material including alternative monomers that are used to replace BPA and clinical practice to reduce BPA exposure during dental treatment. According to (Yuan et al, 2015) dental resin free of bis-GMA should have a better double bond conversion, less shrinkage, comparable flexural strength and modulus, less water solubility, and lower water sorption. Therefore, selecting monomers that are incapable of decomposing into BPA and do not contain BPA as an impurity will aid in the development of BPA-free composites and thus, limiting human exposure (Maserejian et al, 2016).

The latest research successfully developed a second-generation dendrimer, novel dendrimer G(2)-isocyanatoethyl methacrylate (G-IEMA) as an improved formulation of an experimental adhesive in which the G-IEMA in dental adhesives enhances the degree of conversion and shrinkage, helps to increase the immediate dentin bond strength, less nanoleakage expression under the etch and rinse (ER) strategy and its adhesives showed similar behaviour after ageing as 2,2-bis[4-(2-hydroxy-3-methacryloy- loxypropyl)-phenyl]propan (BisGMA) (Vasconcelos et al, 2022). However, further research is required to better understand the usefulness of these dendrimers when hybridizing dentin.

Next, the development of a new hydrophobically modified isosorbide dimethacrylate monomer (ISBGBMA) as a replacement for BisGMA followed in which the corresponding copolymer's degree of conversion, polymerization shrinkage, glass transition temperature, storage modulus, flexural strength, and modulus was similar to those of p(BisGMA/TEGDMA) (Marie et al, 2021). However, clinical trials, either in vivo or in vitro are required to demonstrate the effectiveness of ISBGBMA due to higher water sorption.

Moreover, it has been suggested in a study that the trimethacrylate tris(4-hydroxyphenyl) methane triglycidyl methacrylate (TTM) monomer in combination with TEGDMA, and inorganic fillers demonstrated that the TTM-based composite resin was comparable to the BisGMA/TEGDMA-based composite resin in terms of flexural strength, elastic modulus, degree of conversion, and polymerization shrinkage ($p > 0.05$) (Pérez-Mondragón et al, 2020). However, the levels of water sorption and solubility were statistically higher than the control (p 0.05), but they still met the standards set by ISO 4049 (Pérez-Mondragón et al, 2020).

A fluorinated dimethacrylate (FDMA) monomer was also introduced and synthesized to replace (Bis-GMA) as the base monomer of dental resin due to higher double-bond conversion, lower volumetric shrinkage, and better water resistance (Luo et al, 2016). However, biocompatibility testing is required to determine whether it will affect FDMA-based resin used in clinics and additional studies should be conducted to determine whether FDMA-based materials were resistant to an oral microbial attachment (Luo et al, 2016).

Two new dimethacrylate monomers 5, 5'-methylenedicreosol diglycidyl ether diacrylate (BCF-EA) and 5, 5'-methylenedicreosol diglycidyl ether dimethacrylate (BCF-GMA) derived from renewable bio-based raw materials were synthesized for preparation of dental composites and has a potential alternative matrix to Bis-GMA-based material due to their low cytotoxicity compared to Bis-GMA (Sun et al, 2022). Other than that, the phenyl carbamoyloxy-propane dimethacrylate (PCDMA) also may be used as an alternative to Bis-GMA due to a better degree of cure and less extent of water plasticization (Iliadi et al, 2017).

https://doi.org/10.24191/cos.v11i2.27506 

Tetramethyl bisphenol F acrylate, or TMBPF-Ac, was devised and created in a study to have low viscosity, great mechanical qualities, and biocompatibility and may be utilized as a monomer for dental resin composites, lowering the possibility that people will be exposed to BPA derivatives in the oral environment (Hong et al, 2017). To lessen dietary exposure to Bisphenol A derivatives, a new dimethacrylate monomer, SiMA, was created and used to replace Bis-GMA which had lower water solubility than Bis-GMA/TEGDMA despite having a lower flexural strength (Yuan et al, 2015). However, SiMA-1 still met the ISO requirement (ISO 4049:2009) in flexural strength for polymer-based restorative materials (Yuan et al, 2015).

Another approach in terms of clinical practice and standardized future research methodologies has been made to minimize BPA exposure. As clinically possible, a light-curing tip should be held close to the adhesive (Sifakakis & Eliades, 2017) because the lower the distance light-curing tip to the orthodontic adhesive, the higher the degree of conversion and the lesser the release of BPA. (Sunitha et al, 2011; Purushothaman et al, 2015). Next, the use of pumice as a preventative measure after ortho bonding, indirect irradiation, and mouth washing for the first hour following bonding may all lower the BPA release (Sifakakis & Eliades, 2017). Other than that, the use of rubber dam, (Colombo et al, 2018) increasing suction, increasing air/spray washing, and gargling for 30s after application of dental sealant or composite also may help to reduce BPA exposure during dental treatment (McKinney et al, 2020). Finally, using different materials such as inorganic biomaterials, ceramic (Al-Tannak et al, 2022) and high-viscosity glass-ionomer also would be ideal and healthier for adults and children.

## CONCLUSION

In conclusion, the dental procedure/treatment used a lot of material that contains BPA such as in orthodontic usage, preventive material such as fissure sealant, and in restorative material such as resin-based composites. BPA also can be found in various products such as food packaging that is widely used now, healthcare equipment, thermal paper, toys and articles for children and infants that sometimes can disturb the results of researchers regarding BPA exposure to the human body. From the literature, we found that both short- and long-term BPA exposure are still far below the tolerated daily intake that was set by EFSA in 2015 which is 4 g/kg/day (4000 ng/kg/day). Based on a comparison to the EFSA t-TDI, CENIHR found that oral long-term exposures via dental materials offer low risk to human health. BPA derived from dental products is not a chronic exposure and does not endanger human health.

However, BPA has been shown to play a role in the pathogenesis of several endocrine disorders, including female and male infertility, precocious puberty, hormone-dependent tumors like breast and prostate cancer, and several metabolic disorders, including polycystic ovary syndrome (PCOS). This is resulted from the constant, daily exposure, and its tendency to bioaccumulate in the body. In addition, BPA also affects the respiratory and central neurological systems. There are a few approaches to minimize BPA exposure during the dental procedure such as to hold close the light-curing tip to the adhesive, the use of pumice as a preventative measure after bonding, indirect irradiation, and mouth washing for the first hour following bonding. This may all lower the BPA release. Furthermore, using different materials such as inorganic biomaterials, ceramic and high-viscosity glass ionomer, increasing suction, and air/spray washing, also may help to reduce BPA exposure during dental treatment.

### ACKNOWLEDGEMENTS/FUNDING

The authors are grateful to Universiti Teknologi MARA for the research grant namely DUCS 4.0 (Project Number: 600-UiTMSEL (PI. 5/4) (016/2022)). The authors would also like to thank the Research Management Centre, Universiti Teknologi MARA for the technical support provided.

 

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The authors agree that this research was conducted in the absence of any self-benefits, commercial or financial conflicts and declare the absence of conflicting interests with the funders.

## AUTHORS' CONTRIBUTIONS

Nur Amirah Syafiqah Samsudin and Nur 'Aina Rozainis carried out the research, wrote and revised the article. Zatilfarihian Rasdi conceptualised the central research idea, provided the theoretical framework, and supervised research progress. All authors reviewed the manuscript.

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