VOLUME 11 ISSUE 2 2025

ISSN 2454 – 3055

INTERNATIONAL JOURNAL OF ZOOLOGICAL INVESTIGATIONS

Forum for Biological and Environmental Sciences

Published by Saran Publications, India

International Journal of Zoological Investigations Vol. 11, No. 2, 743-752 (2025)

International Journal of Zoological Investigations

Contents available at Journals Home Page: www.ijzi.net

Editor-in-Chief: Prof. Ajai Kumar Srivastav

Published by: Saran Publications, Gorakhpur, India

ISSN: 2454-3055

The Toxicity-Dynamic Effects of Dioxydiphenylsulfone (BPS) on Particular Human Targets: An *In Silico* Investigation

Sarkar Diptendu[1*], Saha Atanu[2] and Das Kamalesh[3]

[1]Department of Microbiology, Ramakrishna Mission Vidyamandira (An autonomous UG and PG College; Affiliated to University of Calcutta), Belur Math, Howrah 711202, West Bengal, India

[2]Post Graduate Department of Physiology, Hooghly Mohsin College (Affiliated to Burdwan University), College Road, Chinsurah, Hooghly 712101, West Bengal, India

[3]Department of Physiology, Uluberia College (Affiliated to University of Calcutta), Uluberia, Howrah 711315, West Bengal, India

**Corresponding Author*

Received: 7th June, 2025; **Accepted:** 5th August, 2025; **Published online:** 25th October, 2025

https://doi.org/10.33745/ijzi.2025.v11i02.072

Abstract: Dioxydiphenylsulfone (BPS) has been found to disrupt signaling, destroy DNA, and affect the function of android receptors, potentially having both androgenic and antiandrogenic effects. This study aimed to identify BPS's targets in the human system and clarify molecular interactions through molecular docking analysis. The results showed that BPS had major toxicity on the BBB-barrier, Estrogen Receptor Alpha, Estrogen Receptor Ligand Binding Domain, Mitochondrial Membrane Potential, and Cytochrome CYP2C9. Common targets identified included Cyclin-dependent kinase5/CDK5 activator 1, arachidonate 12-lipoxygenase, transthyretin, and Cyclin-dependent kinase 1. Transthyretin (2QPF) and BPS had the best binding energy interaction, according to the docking data (-8.7 Kcal/mol). Cyclin-dependent kinase 5/CDK5 activator 1 (2QKR) and Arachidonate 12-lipoxygenase (3D3I) had the same binding energy with BPS (-8.1 Kcal/mol). Cyclin-dependent kinase 1 had the lowest binding interaction (-7.9 Kcal/mol) (1DKT). This indicates that BPS may negatively impact human physiology, just like BPA does.

Keywords: Dioxydiphenylsulfone, BBB-barrier, Estrogen Receptor Alpha, Mitochondrial Membrane Potential, Cytochrome CYP2C9

Citation: Sarkar Diptendu, Saha Atanu and Das Kamalesh: The toxicity-dynamic effects of dioxydiphenylsulfone (BPS) on particular human targets: An *in silico* investigation. Intern. J. Zool. Invest. 11(2): 743-752, 2025.

https://doi.org/10.33745/ijzi.2025.v11i02.072

Introduction

The chemical description for the organic substance bisphenol S (BPS, dioxydiphenyl-sulfone) is $(HOC_6H_4)_2SO_2$. A sulfonyl group is flanked by 2 phenol functional groups (Angle*et al.,* 2013). In contrast to BPA, BPS has a sulfone group (SO_2) as the main bridge in the chain of molecules rather than bisphenol A's dimethylmethylene group [$C(CH3)_2$]. Considering the spotlight on of

BPA's estrogen-mimicking qualities as well as the general perception that there is sufficient amount of it in the items to be harmful, BPS became a more prevalent chemical component in polyethersulfone along with several epoxies (Medwid *et al.*, 2018; Camacho *et al.*, 2019). BPS could still have hormonal implications that are similar to those of BPA. Due to BPA's proven toxic exposure, producers are increasingly substituting associated chemicals, mostly bisphenol S, for BPA in production processes in order to maintain compliance with limits and laws. Despite the lack of a proven connection involving BPS and cardiovascular illness, it is believed that BPS might operate similarly to BPA therefore prove harmful to the heart (Melnick *et al.*, 2002; Richter *et al.*, 2007; Prins *et al.*, 2018). BPS is being demonstrated to contribute to heart developmental abnormalities along with cardiac arrhythmias within animal experiments. Because BPS triggers the manufacturing of cholesterol in blood vessels, rats receiving excessive amounts of the chemical were shown to have a higher probability of atherosclerosis, an important predictor for heart failure (Vandenberg *et al.*, 2009; Heindel *et al.*, 2020; Sarkar, 2021). There is a possibility that BPS could impact numerous brain processes. The production of thyroid hormone might be affected by BPS ingestion during childbirth, according to a new research report. It has been demonstrated that BPS shortens the neurites in cells that resemble neurons. Subsequently it is believed that BPS's oestrogenic operation, which may disrupt the quantity of thyroid hormone along with function, both of which are critical for healthy growth of the nervous system, is the physiological process underlying harmful neurological effects (Kang *et al.*, 2006; Rubin, 2011; Rochester, 2013; Vandenberg *et al.*, 2014; Lehmler *et al.*, 2018). In past it was suggested that BPS might have had an impact on weight gain, since numerous investigation has linked bisphenol consumption to higher obesity. Obesity is believed to be caused by an increase in lipids in fatty tissue cells, or by the buildup of body fat in the cells that store fat. Extended treatment with BPS results in a better growth of the juvenile bone structure and a stimulation of osteoclast maturation (Volkel *et al.*, 2005; Ye *et al.*, 2011). The newborn's growth spurt may suffer if it is exposed to BPS across the umbilical cord throughout a crucial time. Furthermore, scientists have data which suggests that excessive BPS levels within embryos cause teratogenic consequences on significant organs including as the circulatory system along with liver (Diamanti *et al.*, 2009; Gore *et al.*, 2015; Heindel *et al.*, 2015; Heindel *et al.*, 2020). It has been demonstrated that BPS damages DNA which interferes with signaling. BPS additionally has been demonstrated to influence the action of android receptors, confirming both androgenic as well as antiandrogenic effect. Because of an identified phenol ring, BPA and BPS may act like estrogen (Völkel *et al.*, 2002; Jeng *et al.*, 2011; Nachman *et al.*, 2014).

The present *in silico* study sought to identify the different targets of BPS in the human system and clarify the molecular interaction by molecular docking analysis because BPS, like BPA, has numerous detrimental effects on the human physiological system.

Materials and Methods

Downloading the methyl paraben structure from database:

The chemical structure of dioxydiphenylsulfone (CID: 6626) was downloaded in SDF format from PubChem databse and converted into pdbqt format by using Open Babel 2.3.1 software for further study (Hanioka *et al.*, 2008).

SWISS ADME study:

To aid in developing drugs, this website lets user calculate physicochemical attributes and forecast ADME the variables, pharmacokinetic characteristics, drug like nature, and medicinal chemistry. Friendliness of one or more small compounds can be studied through SWISS ADME server (http://www.swissadme.ch/about.php/). Here, we have uploaded the chemical structure of the compound and finally clicked on analysis to

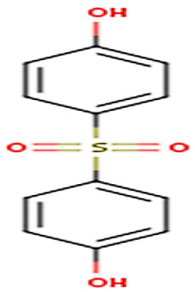

Fig. 1: Chemical structure of BPS (PubChem CID: 6626). Chemical name: dioxydiphenylsulfone. SMILES: C1=CC(=CC=C1O)S(=O)(=O)C2=CC=C(C=C2)O. Molecular formula: $C_{12}H_{10}O_4S$.

obtain detail attributes of the chemicals (Tomza *et al.*, 2017).

Target prediction by SWISS target prediction server and SuperPred 3.0 server:

For predicting the dioxydiphenylsulfone various targets, we used SWISS target prediction sever (http://swisstargetprediction.ch/). Here after uploading the structure and selecting target organism clicked on target prediction and obtained result was downloaded in csv format. Further to get more target related information, we used SuperPred 3.0 server (https://prediction.charite.de/index.php). Here similarly, uploading the structure and selecting target organism clicked on target prediction and obtained result was downloaded in csv format (Benachour *et al.*, 2009).

Systemic toxicity study of Methyl paraben by using Pro Tox 3.0:

For systemic toxicity study model computation was made with the help of Pro Tox 3.0 open server. It has provided complete oral toxicity prediction data including LD_{50} value as well as toxicity score. Here toxicity model prediction results also provided including possible toxicity target (Zoeller *et al.*, 2014).

Molecular docking study:

Auto Dock 4.0 used to fetch ligand scopes respective to protein. First, energy minimized structure fed to working directory, attributed a receptor. Next, dioxydiphenylsulfone referred as ligand. The 'vina.exe', 'split_ligands.exe' and respective license file of the software loaded in working directory. Next, python specific script used to run automated docking, resulting to creation of directory folders (with name of respective ligands) containing a 'log.txt' and a 'out.pdbqt'. Then the splitting function of auto dock vina used to split the 'out.pdbqt' into possible ligand scopes, indexing as 'ligand_1', 'ligand_2' and so on. The interaction results were analysed by Discovery studio software (Matsuda *et al.*, 2012).

Results and Discussion

A nonprofit council of medicine and scientific specialists has determined that bisphenol S (BPS) (Fig. 1) can be harmful to female reproduction. In facilities where bisphenol S is manufactured or utilized, bodily exposure to the chemical can happen by means of particulate breath and direct contact with the skin. According to tracking statistics, people everywhere gets subjected to bisphenol S through food consumption, dust from household appliances being exposed, and skin contact with consumer goods including thermal sheets and banknotes. Polyethersulfone (PES) plastic and rubber particularly can be utilized to create artificial fibers for apparel and other types of fabrics as well as hardened plastic products, contains bisphenol S (BPS) (Watson *et al.*, 2005). As per the oral toxicity prediction by ProTox3.0, the rank of toxicity predicted as 4 out of 6 scale (Table 1, Fig. 2). The LD_{50} value was 1600 mg/kg

Table 1: ProTox-3.0 - Prediction of BPS toxicity

Classification	Target	Shorthand	Prediction	Probability
Toxicity end points	BBB-barrier	bbb	Active	0.69
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Active	1
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Active	1
Metabolism	Cytochrome CYP2C9	CYP2C9	Active	0.5

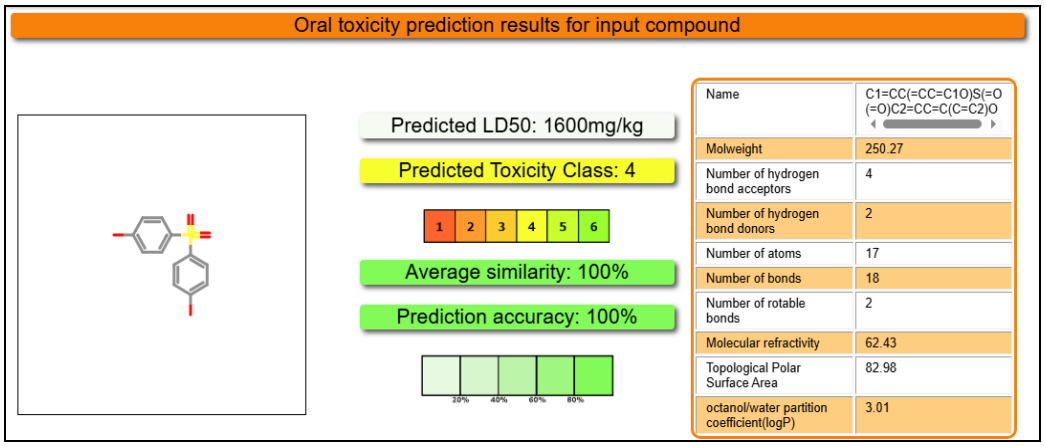

Fig. 2: Oral Toxicity prediction of BPS withProTox 3.0.

and toxicity model prediction was revealed that BPS had the major toxicity (Fig. 3) on the BBB-barrier (probability score 0.69), Estrogen Receptor Alpha (ER) (probability score 1), Estrogen Receptor Ligand Binding Domain (ER-LBD)(probability score 1), Mitochondrial Membrane Potential (MMP)(probability score 0.8) and Cytochrome CYP2C9 (probability score 0.5).

The goal of many different *in silico* techniques is to predict ADME variables based on the structure of the molecules. Notably, Lipinski *et al.*'s ground-breaking study looked at orally active compounds in order to identify physiological ranges that have a high likelihood of becoming an oral medication (i.e. drug-likeness). The connection between pharmacokinetic and physic-chemical characteristics was outlined by this referred to Rule-of-five (Richter *et al.*, 2007). As per the SWISS ADME prediction, molecular weight of the BPS was 250.27 g/mol, number of rotatable bonds present were 2, number of H-bond acceptors were 4, number of hydrogen bond donors were 2, consensus Log Po/w value was 1.88, Log S (ESOL) value was -2.98, GI absorption was found high, Log Kp (skin permeation) value was found as -6.48 cm/s, Bioavailability Score was found as 0.55 and there were no violation of Lipinski, Ghose, Veber, Egan as well as Muegge rules. The SWISS target prediction (Fig. 4) data revealed that there were total 102 numbers of targets in human and most of the target of BPS was enzyme (26.7%), effects on isomerase group of enzymes, kinase group enzymes as well as on transporter system was 13.3%. For oxido-

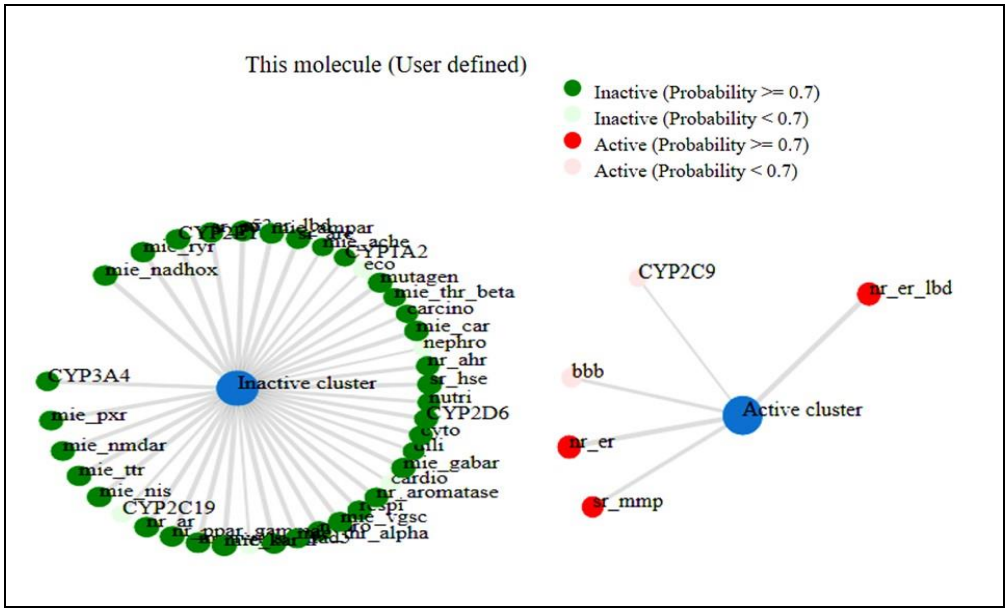

Fig. 3: The network chart from ProTox3.0 (of BPS) is intended to quickly illustrate the connection between the selected compound (BPS) and predicted activities.

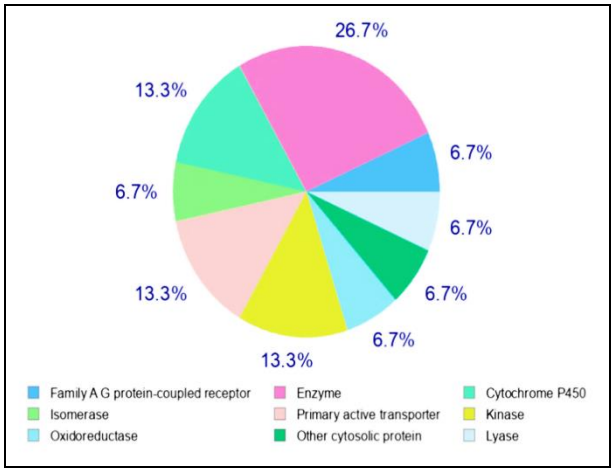

Fig. 4: SWISS target prediction data of BPS.

reductase, different cytosolic proteins, lyase group of enzyme and cytochrome p450 the effects were found as 6.7%. The SWISS ADME prediction, as per the boiled egg (Fig. 5), BPS cannot able to cross blood brain barrier.

Further as per SuperPred 3.0 server prediction, the total number of targets were found as 94 numbers. To extrapolate the common targets predicted in both the open source system, we have used Venny 2.1.0 (https://bioinfogp.cnb.csic.es/tools/venny/) and found that four targets named as Cyclin-dependent kinase 5/CDK5 activator 1, Arachidonate 12-lipoxygenase, Transthyretin and Cyclin-dependent kinase 1 were common (Fig. 6).

Molecular docking helps find high-affinity molecules by predicting the manner in which a ligand is going to attach to a protein. Additionally its binding state or posture forecasts the precise position and direction of the ligand into the protein's engagement pocket (Tomza *et al.*, 2007; Heindel *et al.*, 2015). Comparing this simulated

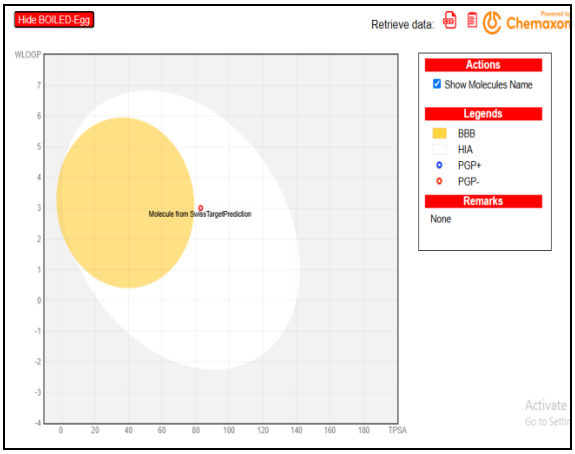

Fig. 5: Boiled Egg information of BPS from the SWISS ADME prediction.

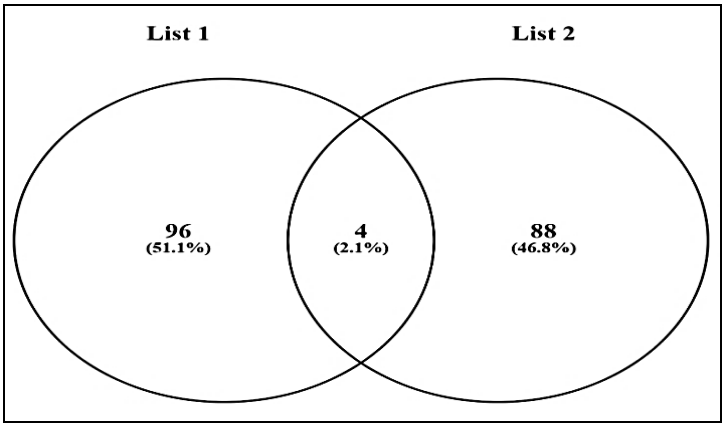

Fig. 6: Venn diagram from SWISS target prediction and SuperPred 3.0 to know the common targets predicted by both the server. The common targets are Cyclin-dependent kinase 5/CDK5 activator 1, Arachidonate 12-lipoxygenase, Transthyretin and Cyclin-dependent kinase 1.

screening method to conventional wet-lab studies, time and resources are saved. All things considered, molecular docking represents an effective technique for supporting pharmaceutical discovery alongside related domains close the disparity between computational forecasts and practical confirmation (Heindel *et al.*, 2020). In this study, to know the interaction with the four common targets i.e. Cyclin-dependent kinase 5/CDK5 activator 1, Arachidonate 12-lipoxy-genase, Transthyretin and Cyclin-dependent kinase 1 along with BPS, we used Auto Dock 4.0 software. Here for docking, crystalized protein structure of Cyclin-dependent kinase 5/CDK5 activator 1 (PDB ID 2QKR), Arachidonate 12-lipoxygenase (PDB ID 3D3I), Transthyretin (PDB ID 2QPF) and Cyclin-dependent kinase 1 (PDB ID 1DKT) were downloaded and prepared for docking. Molecular docking data were further visualized with the help of BioVia discovery studio software. Molecular docking interaction energy was found in between1DKT and BPS was -7.9 Kcal/mol. The interaction residues were TYR 8, ASP 10, LYS 11, ARG 20, TYR 8, LYS 11 and ARG 20. The bonds were involved as Conventional H-bond, pi-cation, Pi-donor (Fig. 7). Cyclin-dependent kinase 1 (CDK1), also known as cell division cycle protein 2 homolog (Cdc2), is a serine/threonine kinase that is crucial for regulating the cell cycle, particularly the transition from G2 phase to mitosis (Lehmler *et al.*, 2018). Cdk1 is heavily regulated because of its crucial

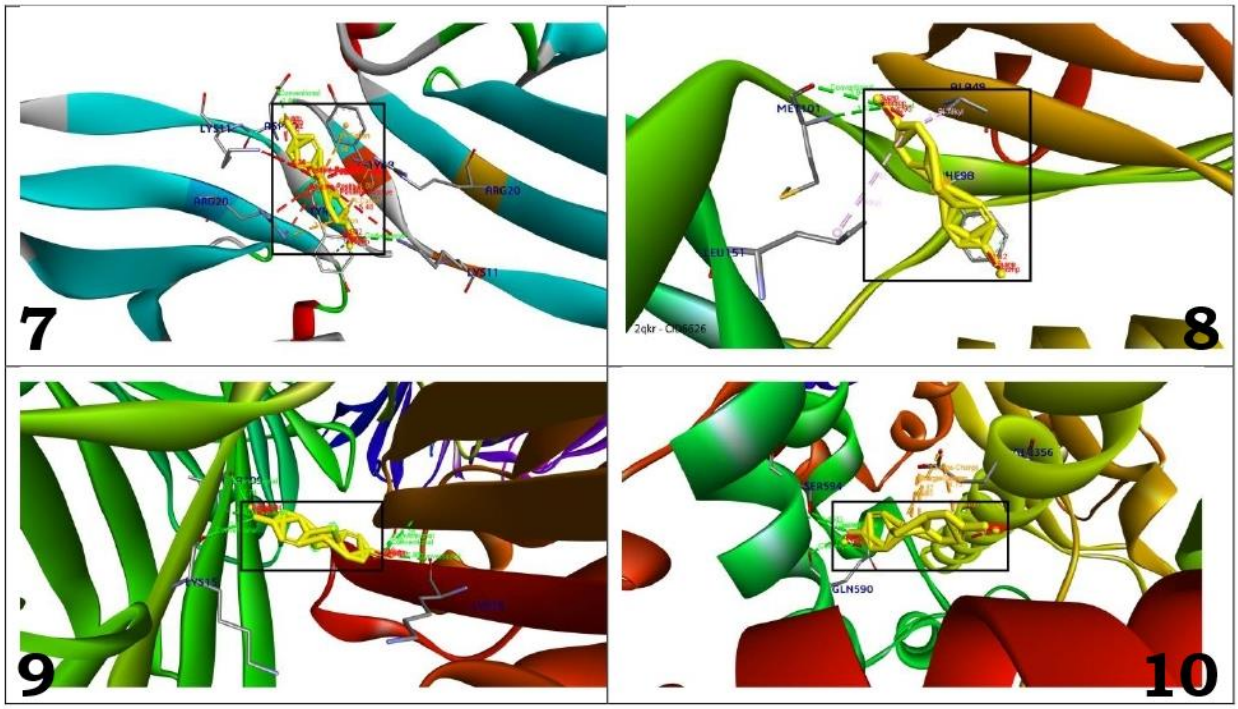

Fig. 7: Molecular docking interaction between1DKT and BPS. The interaction energy was found -7.9 Kcal/mol.
Fig. 8: Molecular docking interaction between 2QPF and BPS. The interaction energy was found -8.7 Kcal/mol.
Fig. 9: Molecular docking interaction between 2QKR and BPS. The interaction energy was found -8.1 Kcal/mol.
Fig. 10: Molecular docking interaction between 3D3I and BPS. The interaction energy was found -8.1 Kcal/mol.

function in the course of the cell cycle. The most evident way that Cdk1 is controlled is by its binding to cyclin partners. Cyclin engagement modifies access to Cdk1's active site, enabling Cdk1 activity; moreover, cyclins give Cdk1 functional selectivity (Hanioka *et al.*, 2008). A hydrophobic patch found in at least some cyclins may interact directly with substrates to provide target selectivity. Moreover, Cdk1 can be directed by cyclins to specific subcellular sites. Molecular docking interaction energy was found in between 2QKR and BPS was -8.1 Kcal/mol. The interaction residues were ALA 49, MET 101, PHE 98 and LEU 151. The bonds were involved as Conventional H-bond, pi-cation, Pi-alkyl (Fig. 8). CDK5 promotes the growth of lymphatic vessels. CDK5 phosphorylates Foxc2, a protein gene that regulates the production of connexin 37, which is necessary for the formation of lymphatic channels (Vandenberg *et al.*, 2009; Gore *et al.*, 2015). For the central nervous system to develop properly, CDK5 must be activated. By extending the stimulation and altering its cellular place of residence, P25 opens up CDK5 expression (Volkel *et al.*, 2005; Kang *et al.*, 2006). Molecular docking interaction energy was found in between 2QPF and BPS was -8.7 Kcal/mol. The interaction residues were LYS 15, ALA 109, LYS 15 and ALA 109. The bonds were involved as only Conventional H-bond (Fig. 9).The TTR gene, found on the long arm of chromosome 18, encodes the human transthyretrin protein. Thyroid hormone (thyroxine) along with retinol (vitamin A) are transported by transthyretin (TTR), sometimes referred to as prealbumin, a protein which is mostly made in the hepatic system. Being composed of four subunits that are all alike, it is a triplet (Rochester, 2013; Gore *et al.*, 2015). Transthyretin amyloidosis (ATTR) is a disorder caused by amyloid deposits in different organs as a result of TTR fold errors or

abnormalities (Richter *et al.*, 2007). Molecular docking interaction energy was found in between 3D3I and BPS was -8.1 Kcal/mol. The interaction residues were GLN 590, SER 594 and GLU 356. The bonds were involved as Conventional H-bond, Pi-anion, charge-charge (Fig. 10). Arachidonic acid and linoleic acid are examples of polyunsaturated fatty acids that are oxygenated by lipoxygenases (LOXs). According to the identification of its mRNA, human ALOX12 resides mainly in blood platelets, especially leukocytes, although smaller amounts being discovered in the pancreatic islets of Langerhans, the basal layer of the epidermis (particularly in psoriasis skin blisters), and some types of malignancies (Benachour *et al.*, 2009; Heindel *et al.*, 2015). So, as per the docking data, the best interaction in terms of binding energy was found in between Transthyretin (2QPF) and BPS. Same binding energy were found both for Cyclin-dependent kinase 5/CDK5 activator 1 (2QKR) and Arachidonate 12-lipoxygenase (3D3I) with BPS. Least binding interaction was found for Cyclin-dependent kinase 1 (1DKT).

Conclusion

There is no evidence linking dioxydiphenylsulfone (BPS) to cardiovascular disease, It has been established that BPS disrupts signaling and destroys DNA. Furthermore, it has been shown that BPS affects android receptors function, confirming both an androgenic and an antiandrogenic impact. The discovered phenol ring in BPA and BPS may cause them to behave similarly to estrogen. Because BPS, like BPA, has many negative impacts on the human physiological system, the current *in silico* study aimed to identify the various targets of BPS in the human system and clarify the molecular interaction by molecular docking analysis. The LD_{50} value was 1600 mg/kg, and the toxicity model prediction showed that BPS had the major toxicity on the BBB-barrier (probability score 0.69), Estrogen Receptor Alpha (ER) (probability score 1), Estrogen Receptor Ligand Binding Domain (ER-LBD) (probability score 1), Mitochondrial Membrane Potential (MMP) (probability score 0.8), and Cytochrome CYP2C9 (probability score 0.5). ProTox3.0 predicted the rank of toxicity as 4 out of 6 scale. The SWISS target prediction data showed that there were 102 targets in total, however, the SuperPred 3.0 server forecast showed 94 targets in total. Cyclin-dependent kinase 5/CDK5 activator 1, arachidonate 12-lipoxygenase, transthyretin, and Cyclin-dependent kinase 1 were identified as the four common targets. Transthyretin (2QPF) and BPS had the best binding energy interaction, according to the docking data (-8.7 Kcal/mol). Cyclin-dependent kinase 5/CDK5 activator 1 (2QKR) and Arachidonate 12-lipoxygenase (3D3I) had the same binding energy with BPS (-8.1 Kcal/mol). Cyclin-dependent kinase 1 had the lowest binding interaction (-7.9 Kcal/mol) (1DKT). This demonstrates that BPS, like BPA, may have detrimental effects on human physiology.

Ethical Statement

The authors confirm that all ethical issues have been dealt with the research ethics guidelines provided by the Department of Microbiology, Ramakrishna Mission Vidyamandira, Belur Math, Howrah, West Bengal, India.

Author Contributions

Each author has contributed equally to the study's planning, analysis, writing, and editing. All authors have read and agreed to the published version of the manuscript.

Acknowledgements

Authors are grateful to the Department of Biotechnology (DBT), Government of India, for granting open support in Financial and Educational aspiration.

Conflict of Interest

The authors declare no conflicts of interest.

References

Angle BM, Do RP, Ponzi D, Stahlhut SW, Drury BE, Nagel SC, Welshons WV, Besch-Williford CL, Palanza P, Parmigiani S, Saal FSV and Julia A. (2013) Taylor

Metabolic disruption in male mice due to fetal exposure to low but not high doses of bisphenol A (BPA): Evidence for effects on body weight, food intake, adipocytes, leptin, adiponectin, insulin and glucose regulation. Reprod Toxicol. 42: 256-268.

Benachour N and Aris A. (2009) Toxic effects of low doses of bisphenol-a on human placental cells. Toxicol Appl Pharmacol. 241(3): 322-328.

Camacho L, Lewis SM, Vanlandingham MM, Olson GR, Davis KJ, Patton RE, Twaddle NC, Doerge DR, Churchwell MI, Bryant MS, McLellen FM, Woodling KA, Felton RP, Maisha MP, Juliar BE, Gamboa da Costa G and Delclos KB. (2019) A two-year toxicology study of bisphenol A (BPA) in Sprague-Dawley rats: CLARITY-BPA core study results. Food Chem Toxicol. 132: 110728.

Diamanti KE, Bourguignon JP, Giudice LC, Hauser R, Prins GS, Soto AM, Zoeller RT and Gore AC. (2009) Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocr Rev. 30(4): 293-342.

Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, Prins GS, Toppari J and Zoeller RT. (2015) EDC-2: The Endocrine Society's second scientific statement on endocrine-disrupting chemicals. Endocr Rev. 36(6): E1-E150.

Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, Prins GS, Toppari J and Zoeller RT. (2015) EDC-2: The Endocrine Society's second scientific statement on endocrine-disrupting chemicals. Endocr Rev. 36(6): E1-E150.

Hanioka N, Naito T and Narimatsu S. (2008) Human UDP-glucuronosyltransferase isoforms involved in bisphenol A glucuronidation. Chemosphere 74(1): 33-36.

Heindel JJ, Belcher S, Flaws JA, Prins GS, Ho SM, Mao J, Patisaul HB, Ricke W, Rosenfeld CS, Soto AM, Vom Saal FS and Zoeller RT. (2020) Data integration, analysis, and interpretation of eight academic CLARITY-BPA studies. Reprod Toxicol. 98: 29-60.

Heindel JJ, Newbold RR, Bucher JR, Camacho LC, Delclos KB, Lewis SM, Vanlandingham M, Churchwell MI, Twaddle NC, McLellen M, Chidambaram M, Bryant M, Woodling K, Costa GG da, Ferguson SA, Flaws J, Howard PC, Walker NJ, Zoeller RT, Fostel J, Favaro C and Schug TT. (2015) NIEHS/FDA CLARITY-BPA research program update. Reprod Toxicol. 58: 33-44.

Jeng YJ and Watson CS. (2011) Combinations of physiologic estrogens with xenoestrogens alter ERK phosphorylation profiles in rat pituitary cells. Environ Health Perspect. 119(1): 104-112.

Kang JH, Kondo F and Katayama Y. (2006) Human exposure to bisphenol A. Toxicology 226(2-3): 79-89.

Lehmler HJ, Liu B, Gadogbe M and Bao W. (2018) Exposure to bisphenol A, bisphenol F, and bisphenol S in U.S. adults and children: The National Health and nutrition examination survey 2013-2014. ACS Omega 3(6): 6523-6532.

Matsuda S, Matsuzawa D, Ishii D, Tomizawa H, Sutoh C and Nakazawa K. (2012) Effects of perinatal exposure to low dose of Bisphenol A on anxiety like behavior and dopamine metabolites in brain. Progress Neuro-Psychopharmacol Biol Psychiatry 39(2): 273-279.

Medwid S, Guan H and Yang K. (2018) Bisphenol A stimulates adrenal cortical cell proliferation via ERβ mediated activation of the sonic hedgehog signaling pathway. J Steroid Biochem Mol Biol. 178: 254-262.

Melnick R, Lucier G, Wolfe M, Hall R, Stancel G, Prins G, Gallo M, Reuhl K, Ho S, Brown T, Moore J, Leakey J, Haseman J and Kohn M. (2002) Summary of the National Toxicology Program's report of the endocrine disruptors low-dose peer review. Environ Hlth Perspect. 110(4): 427-431.

Nachman RM, Hartle JC, Lees PSJ and Grropman JD. (2014) Early life metabolism of bisphenol A: A systematic review of the literature. Curr Environ Hlth Rep. 1(1): 90-100.

Prins GS, Hu WY, Xie L, Shi GB, Hu DP, Birch L and Bosland MC. (2018) Evaluation of bisphenol A (BPA) exposures on prostate stem cell homeostasis and prostate cancer risk in the NCTR-Sprague-Dawley rat: An NIEHS/FDA CLARITY-BPA consortium study. Environ Hlth Perspect. 126(11): 117001.

Richter CA, Taylor JA, Ruhlen RL, Welshons WV and Vom Saal FS. (2007) Estradiol and Bisphenol A stimulate androgen receptor and estrogen receptor gene expression in fetal mouse prostate mesenchyme cells. Environ Hlth Perspect. 115(6): 902-908.

Rochester JR. (2013) Bisphenol A and human health: A review of the literature. Reproductive Toxicol. 42: 132-155.

Rubin BS. (2011) Bisphenol A: An endocrine disruptor with widespread exposure and multiple effects. J Steroid Biochem Molec Biol. 127(1-2): 27-34.

Sarkar D. (2021) Molecular Docking study to identify potent fungal metabolites as inhibitors against SARS-CoV-2 main protease enzyme. Int J Pharm Bio Sci. 12(2): 78-85.

Tomza MA, Stepkowska P, Kuba J and Pilarczyk B. (2017) Effect of bisphenol A on reproductive processes: A review of in vitro, in vivo and epidemiological studies. J Appl Toxicol. 38(1): 51-80.

Vandenberg LN, Hauser R, Marcus M, Olea N and Welshons WV. (2007) Human exposure to bisphenol A (BPA). Reproductive Toxicol. 24(2):139-177.

Vandenberg LN, Maffini MV, Sonnenschein C, Rubin BS and Soto AM. (2009) Bisphenol-A and the great divide: A review of controversies in the field of endocrine disruption. Endocrine Rev. 30(1): 75-95.

Volkel W, Bittner N and Dekant W. (2005) Quantitation of bisphenol A and bisphenol A glucuronide in biological samples by high performance liquid chromatographytandem mass spectrometry. Drug Metabolism Disposition 33(11): 1748-1757.

Völkel W, Colnot T, Csanády GA, Filser JG and Dekant W. (2002) Metabolism and kinetics of bisphenol A in humans at low doses following oral administration. Chem Res Toxicol. 15(10):1281-1287.

Watson CS, Bulayeva NN, Wozniak AL and Finnerty CC. (2005) Signaling from the membrane via membrane estrogen receptor-alpha: estrogens, xenoestrogens, and phytoestrogens. Steroids 70(5-7): 364-371.

Ye X, Wong L-Y, Bishop AM and Calafat AM. (2011) Variability of urinary concentrations of bisphenol A in spot samples, first morning voids, and 24-hour collections. Environ Hlth Perspect. 119(7): 983.

Zoeller RT, Bergman Å, Becher G, Bjerregaard P, Bornman R, Brandt I, Iguchi T, Jobling S, Kidd KA, Kortenkamp A, Skakkebaek NE, Toppari J and Vandenberg LN. (2014) A path forward in the debate over health impacts of endocrine disrupting chemicals. Environ Hlth. 13(1): 118.