RiAT
Revista Interamericana de Ambiente y Turismo
Interamerican Journal of Environment and Tourism
Print version ISSN - 0717 - 6651, Online version ISSN - 0718 - 235X
http://dx.doi.org/10.4067/S0718-235X2021000200179
http://riat.utalca.cl
www.fen.utalca.cl

Research paper

The cellulose industry and its impact on the population: From the social to the biochemical

La industria de la celulosa y su impacto en la población: Desde lo social a lo bioquímico

Matías González[1*], Violeta Morin[2*], Nicolás Labra[3] , Ariel Castro[4]

[1] M. Sc., Proteases and Cancer laboratory, Faculty of Biological Sciences, University of Concepción, Concepción, Chile
[2] Ph.D. in Biological Sciences, Proteases and Cancer laboratory, Faculty of Biological sciences, University of Concepción, Concepción, Chile
[3] Ph.D student, Tyndall Centre for Climate Change Research, University of Manchester, Manchester, UK
[4] Ph.D. in Biological Sciences, Signal Transduction and Cancer laboratory, Faculty of Biological sciences, University of Concepción, Concepción, Chile
* Corresponding author: matiasivan.gh@gmail.com

Received: 2021-08-15 Accepted for publication: 2021-11-14 Published: 2021-12-30

ABSTRACT

The Biobío region in Chile is characterized by a strong forestry industry, which provides jobs and supports regional GDP. Cellulose production is one of the most economically relevant activities, but it causes environmental, social, and public health problems. The generation of polycyclic organic compounds in cellulose production is one of the primary pollutants. It can produce endocrine effects and DNA alteration through interaction with enzymes of the CYP family and Aryl hydrocarbon receptors, affecting organisms' functioning. Retene is one of the polycyclic aromatic organic compounds generated in cellulose production. However, its harmful potential for human health remains poorly explored. From another perspective, the circular economy seeks to use production waste as inputs. However, cellulose contaminants are found in traces, resulting in a limitation for promoting a valorization industry. Under a reduction approach, there is a potential to improve production processes that increase retene and form other organic compounds, thus preventing cellulose contaminants from entering the environment. This review approaches the environmental problem from an interdisciplinary perspective, to highlight biochemistry and circular economy in order to determine and solve a priori environmental problems.

Keywords: *wastewater pollution, polycyclic aromatic hydrocarbons, environmental pollution, pull mill, endocrine disruptors.*

RESUMEN

La región del Biobío en Chile posee una fuerte industria forestal, que genera empleos y sostiene el PIB regional. La producción de celulosa es una de las actividades más relevantes económicamente, generando problemas ambientales, sociales y de salud pública. La generación de compuestos orgánicos en la producción de celulosa es uno de los principales contaminantes pudiendo producir efectos endocrinos y alteración del ADN a través de la interacción con enzimas de la familia CYP y receptores de hidrocarburos arilo, afectando el funcionamiento de los organismos. El Reteno es uno de los compuestos generados en la producción de celulosa. Sin embargo, su potencial efecto para la salud humana sigue siendo poco conocido. Desde otra perspectiva, la economía circular busca utilizar los residuos de la producción como insumos. Sin embargo, los contaminantes de celulosa se encuentran en trazas, lo que resulta en una limitante para promover una industria de valorización. Bajo un enfoque reduccionista, se pueden mejorar el proceso de producción que aumentan el reteno y forman otros compuestos orgánicos, evitando así que los contaminantes de celulosa ingresen al medio ambiente. Esta revisión aborda el problema ambiental desde una perspectiva interdisciplinaria, con el fin de determinar y resolver problemas ambientales a priori.

Palabras clave: Hidrocarburos aromáticos policíclicos, contaminación ambiental, celulosa .

1. INTRODUCTION

The pollution of freshwater bodies is not exclusively a local problem, but rather a global one. The cellulose industry is a profitable business that grows every year worldwide. It is one of the main activities responsible for water resources deterioration due to the amount of water required for the process and the amount of liquid industrial waste it generates, ranking globally as the sixth largest industrial generator of liquid pollutants (Uğurlu et al., 2008; Simão et al., 2018; Singh & Chandra, 2019).

Forestry sector operations in Chile have not been far from this reality. The Chilean forestry industry dates back to Spanish colonization in the 16th century, undergoing an intense modernization process in the last fifty years (Donoso & Otero, 2005; Camus & Solari, 2008). In 2018, the forestry sector contributed $US 4.581 billion annually to the country's gross domestic product (GDP), of which $US 4.277 billion came from cellulose production. This generated 113,769 jobs, of which 7,765 correspond to employees linked to cellulose production (Gysling et al., 2019). In the same year, $US 3.66 billion were exported, mainly to China,

South Korea, and the Netherlands (Gysling et al., 2019). The forestry industry's increased relevance has resulted in a series of economic expansion policies dating back to the 1970s. This expansion has generated a high presence of corporations associated with cellulose production in Chile and South America. Their operations have had environmental effects and also affected a socio-cultural level by excluding surrounding social actors. The most recognized effect occurred in 2005 when there was a significant decrease in the population of black-necked swans in Valdivia due to the waste dumped by the Arauco pulp mill in the Cruces River (Ehrnström-Fuentes, 2015; Ehrnström-Fuentes & Kröger, 2017). As an approach that seeks to minimize the socio-environmental impacts of production processes, the Circular Economy (CE) has acquired prominence as demonstrated through public policies and research centers promising to affect all industrial sectors. In this context, it is interesting to establish a first analysis that allows the exploration of CE offers for the cellulose case, accompanied by a biochemical perspective aiming to understand the effect of production on the population.

1.1 Context of the forest industry in the Biobío region

In the Biobío region, the industry dedicated to cellulose production is found mainly in the basin of the Biobío River, which runs between 36°45'S; 72°59' W and 38°20'S; 71°15' W with a length of 380 Km, from headwaters in the Icalma and Galletué lakes in the Andes Mountains (Orrego et al., 2006). The Biobío River receives 100000 tons per year of wastewater from the cellulose industry, containing residues from pulp production and paper manufacture based on monoculture forest species Pinus radiata and Eucalyptus nitens (Videla & Diez, 1997; Orrego et al, 2006). The Biobío River basin is a complex system because of its diversity and because 5% of its population belongs to the indigenous Mapuche ethnic group. On a national level, the Biobío River is of great importance for economic development. Apart from the cellulose industry, farms, industrial refineries and hydroelectric plants also use the river. Therefore, the Biobío River Basin represents a complex mosaic of activities, inhabitants, and biological diversity (Díaz et al., 2018). It is important to note that there are five cellulose production plants in the Biobío region (Table 1). These plants impact the area's industrialization and employment rates. They contribute 15.8% of the forest GDP and generate 7,765 jobs (Salas et al., 2016; Gysling et al., 2019). However, they also impact the native state of the river in terms of its composition since the waste originated in the production process will directly alter these industries' environmental dynamics.

Table 1. Cellulose production plants in the Biobío region (Gysling et al., 2019).

Pulp mill plant	class	Production (tons)	Location (Commune)
BO Paper Bío-Bío SA	Thermo-mechanical	125000	San Pedro de la Paz
Celulosa Arauco y Constitución S.A	Chemical	790000	Arauco
CMPC Pulp SPA	Chemical	330000	Laja
CMPC Pulp SPA	Chemical	1500000	Nacimiento

2. LIQUID INDUSTRIAL WASTE FROM CELLULOSE PRODUCTION

The liquid waste from cellulose production has a contaminant load based on the contribution of suspended solids from biodegradable organic matter. This figure is measured as biological oxygen demand (BOD5) in the order of 744 mgL-1 to 400 mgL-1 according to samples obtained from two effluents near the Biobío River (Gaete et al., 2000). The cellulose industry has introduced improvements to reduce the BOD5 rates, integrating physical-chemical treatments to eliminate suspended solids (SS) and biological treatments to reduce organic matter (Chamorro et al., 2013). However, certain compounds resist biological treatment. They are present in the wastewater that goes to the receiving bodies, intervening in various organisms' physiology and metabolism (Gaete & Paredes, 1996; Gaete et al., 2000; Orrego et al., 2006; Chiang et al., 2015). The characterization of the liquid industrial wastes originating from cellulose production is problematic since these wastes constitute a complex matrix of organic compounds. We can find compounds usually present in nature, such as tannins, resin acids, lignin, phytohormones, phytosterols, and stilbenes. Simultaneously, we have compounds that originate in the production process and enter the environment as exogenous elements known as xenobiotics (Top & Springael, 2003). The Xenobiotics found in the residues of the cellulose production process include chlorinated lignins, phenols, dioxin, polychlorinated dibenzodioxins, benzo[A]pyrene (B[a]P), benzoanthracenes, benzoflavones, and retene, among other polycyclic aromatic hydrocarbons (PHA) (Ali & Sreekrishnan, 2001; Lahdelma & Oikari, 2005; Hernández et al., 2013; Murray et al., 2014). Xenobiotics have an anthropogenic origin and are molecules that enter the environment in higher concentrations than natural ones (Top & Springael, 2003). When discharged into rivers, these molecules form sediment. The benthos retains and progressively releases the contaminants, expanding the species inhabiting this particular environment and inducing molecular machinery expression that metabolizes these compounds and maintains cellular homeostasis.

In general, xenobiotics altering the normal functioning of organisms are called endocrine disruptors (ED). They directly alter the production, delivery, and metabolism of some hormones, or through a functional mimicry effect, produce epigenetic changes in subsequent generations and obesity problems (Birkett & Lester, 2002; Anway & Skinner, 2006; Casals-Casas & Desvergne, 2011; Darbre, 2017). Xenobiotics can enter the cell by passive transport (Fig.1). For example, once in the cytosol, PHA binds to the Aryl hydrocarbon receptor (AHR), triggering a signal that will end in the expression of the Cytochrome P450 (CYP) protein. The AHR receptor belongs to the subfamily of transcription factors called bHLH (basic Helix-Loop-Helix). It forms a cytosolic complex with the 90-kDa heat shock protein (HSP90) and hepatitis B virus X-associated protein 2 (XAP2) (Plant et al., 1987; Beischlag et al., 2008). The xenobiotic binds to AHR as an agonist. Then, the xenobiotic-AHR complex migrates to the nucleus, forming a dimer with the aryl hydrocarbon receptor nuclear translocator (ARNT) and dissociating from the HSP90 and XAP2 proteins (Bersten et al., 2013; Murray et al., 2014). ARNT leads the protein/ligand complex, formed by polycyclic hydrocarbon and AHR, to regions of the DNA called dioxin response elements (DRE) (Murray et al., 2014). DRE are consensus sequences found upstream of genes expressed by dioxins. The AHR/ARNT/ligand complex binds to the DRE sequences hosted in gene-promoting regions such as CYP1A1 (Li et al., 2014), promoting the expression of enzymes required for degradation of xenobiotic compounds. The cytochrome P450 enzyme (CYP) is a highly conserved hemoprotein in the animal kingdom, which uses NADPH as a cofactor. It participates in the degradation of xenobiotic compounds by catabolizing mono-oxidation reactions (Fujii-Kuriyama & Mimura, 2005). CYP is a superfamily that includes more than 13,000 genes grouped in 400 families. In Homo sapiens, at least 57 genes and 58 pseudogenes grouped in 18 families and 44 subfamilies have been documented. Families 1-3 of CYP are the most active, and their expression and activity are concentrated in the liver to metabolize organic compounds (Manikandan & Nagini, 2018). Therefore, these enzymes are useful molecular biomarkers of environmental quality since they are overexpressed by organisms exposed to xenobiotics in their environment. Environmental and toxicology studies widely use the measurement of the activity or expression of CYP isoforms(Hong & Yang, 1997; Fujita et al., 2001; Takano et al., 2002; Buratti et al., 2003; Räsänen et al., 2012; Jansen van Rensburg et al., 2019; Vähäkangas et al., 2019) After PHA metabolization, epoxies can form, pass from the cytoplasm into the nucleus and react with the DNA, generating what is known as an adduct. The adduct is formed from covalent bonds of the benzyl carbon of the xenobiotic and the amino group of deoxyadenosines and deoxyguanosine residues (Essigmann et al, 1977; Massion et al, 2016; Barnes et al, 2018; Estévez et al, 2019). When the DNA replicates, the adducts' interference results in mutations with the potential to develop neoplasms (Denissenko et al, 1996; Hecht, 1998; Szeliga & Dipple,1998; Vineis and Perera, 2000; Tarantini et al., 2011; Poirier, 2016).

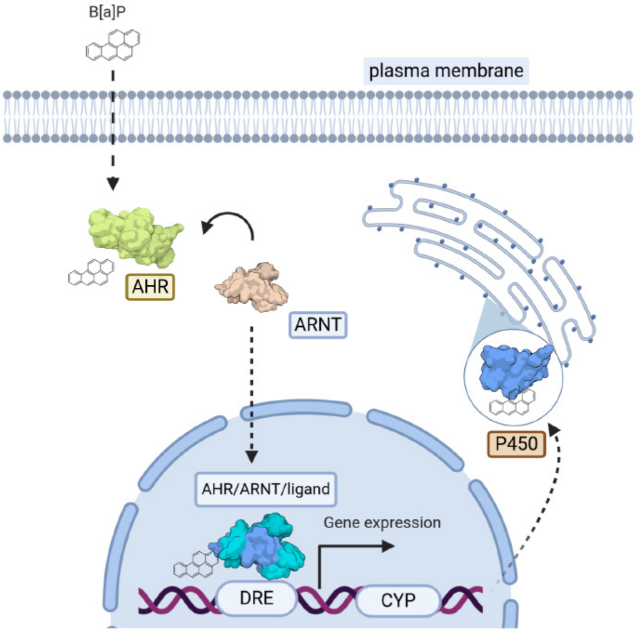

Figure 1. Diagram of the Cytochrome P450 expression induced by polycyclic aromatic hydrocarbons such as Benzo[a]pyrene. PHA enters the cell by facilitated transport. It promotes the expression of genes of the CYP1A and CYP1B family through coordination between the Aryl hydrocarbon receptor, the Aryl hydrocarbon translocator, and the xenobiotic. This complex translocates to the nucleus where it binds to dioxin response sequences upstream of the CYP genes, being a regulatory transcription factor in CIS.

3. HUMAN HEALTH RISKS ASSOCIATED WITH RETENE

Retene (1-methyl-7-isopropyl phenanthrene) is a polycyclic organic compound formed from abiatane skeletons by combustion processes, such as wood burning. For this reason, it is a molecular marker of environmental pollution. When subjected to high-temperature thermal processes, this compound is reduced and generally transformed into retene and is considered like a new compound toxic for metabolism (Ramdahl, 1983; Marchand-Geneste & Carpy, 2003; Diniz et al., 2010). Retene has been found in lakes and sediments without anthropogenic activity in concentrations of nanograms to micrograms per dry gram of sediment by bacterial aromatization of abiatic acid (Zender et al, 1994; Billiard et al, 1999). This concentration increases by many orders of magnitude in sediments located downstream from liquid industrial waste discharge originating from cellulose production, reaching concentrations of 1330 μgg-1(Lahdelma & Okari, 2005; Räsänen et al., 2012).

Studies on aquatic vertebrates, such as Danio rerio, Oncorhynchus mykiss and Xenopus Tropicalis, associated retene and other aromatic compounds, such as Benzo[a] Pyrene, with disruptive activity on several processes, including apoptosis, teratogenesis, cell growth, cell adhesion and mobility, cardiovascular development, xenobiotic metabolism, lipid transport and metabolism, and amino acid metabolism (Regnault et al., 2018).

These compounds are closely related to the expression of CYP1A genes by binding to the AHR and show dioxin-like toxic behavior (Gelboin, 1980; Billiard et al., 2002; Oikari et al., 2002; Hawliczek et al., 2012: Regnault et al., 2018). Few studies have been done on the effect of retene in humans, partly because it is not on the PHA list that the United States Environmental Protection Agency (US-EPA) monitors for compounds with carcinogenic potential (Jarvis et al., 2014). Cytotoxicity has been demonstrated in human lung cells treated with 30 ngml-1 retene for 72 hours, and subsequent experiments have shown retene-induced cell death and oxidative stress (de Oliveira Alves et al., 2017; Peixoto et al., 2019). In the hepG2 liver cell line, retene is metabolized in 24 hours through the ortho-quinone route, where the cytochrome P450 protein expression is also stimulated (Huang et al., 2017).

Retene and several other PHAs are not regulated by Chilean legislation; furthermore, there are no constant updates based on regulations of other countries (DS 609/1998, MOP; DS 90/2000, SEGPRES; DS 148/2003, MINSAL). According to all this biochemical context, from a normative point of view, environmental legislation is lax. Additionally, the lack of innovation spaces has generated an organizational culture that focuses only on treating downstream cellulose production pollutants. However, the potential scale of pulp industry impacts on natural ecosystems and human sites, along with consumers demanding better production standards, necessitates the application of cross-cutting approaches to minimization, such as the Circular Economy.

4. CIRCULARITY STRATEGIES

Circular Economy (CE) is currently positioned as one of the most relevant principles of industrial ecology, promoting the decoupling of economic growth and socio-environmental impact. At the productive level, the objective of CE is to minimize waste generation, especially those wastes which do not present alternatives to recovery. A CE-based approach takes natural cycles as its technical references. Each material or energy flow is integrated as a recoverable component within other natural systems. CE has been interpreted through a hierarchy of circular strategies in waste management, extending to a maximum of 10 strategies (Figure 2). Systems that focus on the higher hierarchy strategies are preferable because they involve minimal or nonexistent natural resource extraction. In the cellulose industry and particularly for retene, two main constraints make the implementation of CE strategies difficult. The first is related to the microscopic retene concentrations, making its identification and extraction difficult. The second is based on the state of the art of polycyclic aromatic hydrocarbon valorization. At present, no processes have been identified in which retene and other similar organic components originating from cellulose production processes can be used as input.

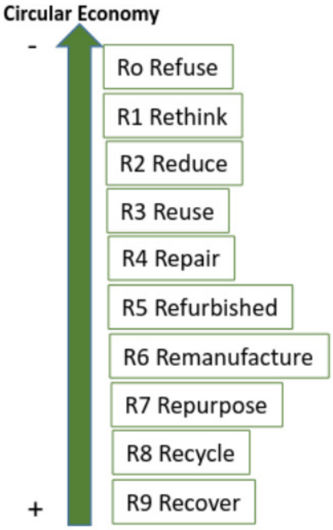

Figure 2. CE hierarchy according to Potting et al., 2017

Only wastewater recycling and industrial symbiosis strategies have been used in European countries such as Sweden and Norway (Molina-Sánchez et al, 2018; Domenech et al, 2019). For both limitations, the promotion of research lines to explore detection and valorization methods is a critical element that can add value to the industry. Despite these limitations, the CE hierarchy offers two relevant foci to minimize the environmental, social, and economic impact of the cellulose production cycle. The first is associated with the Reduction strategy that can succeed by improving processes. In particular, the control of the thermal processes, to reach complete combustion, would allow an early decrease in retene production (Simoneit, 2002). The second focus corresponds to the reprocessing of cellulose products through recycling, considering that the combustion stage that occurs in the recycling stages is not directly associated with the production of retene, although it is related to other highly persistent compounds, such as resin acids (Rigol et al., 2002; Terasaki, 2008). If the generation of pollutants from recycling were lower than in the industry that uses virgin material, this would further enhance an iconic industry characterized by its maturity and scope. In Chile, paper and cardboard recycling alone leads the rates per material with 80% (Pacto Global, 2015). Notably, the use of paper and cardboard to generate new cellulose products avoids the extraction of forest resources and, therefore, the socio-environmental conflicts associated with their exploitation.

5. CONCLUSIONS

In the BioBio region of Chile, deaths and mortality rates since 2000 show an increasing trend (MINSAL, 2011; Itriago et al., 2013). Environmental risk factors affecting the prevalence of some types of cancer are associated with economic activity, mainly the forestry and agricultural industry, exposing the population to residual chemicals (Itriago et al., 2013). Based on this, it is urgent to study the possible impacts on human health from liquid industrial waste PHAs, particularly retene. On the other hand, environmental pollution is not restricted to the empirical determination of the effects of a particular compound on human health or its impact on the environment. Still, it acquires a much greater value when the problem is addressed from its socio-cultural context since it originates from this context. Scientific alignment in environmental matters must go hand in hand with applying new technologies, such as mass sequencing and spectroscopy. These technologies can determine the metabolic pathways and possible a priori impacts of compounds originating in cellulose production, and in the industry at large, to adopt precautionary measures. The concentration at the trace level, together with the lack of productive processes that use retene and other polycyclic organic compounds as inputs, makes it difficult for CE to minimize environmental impacts. However, a macro analysis allows us to reinforce the importance of improving combustion processes and paper and cardboard recycling benefits. For the latter, other studies are needed to compare the generation of a broader range of pollutants in both cellulose production lines (virgin material vs. recycling) to minimize the impact on public, environmental and social health.

ACKNOWLEDGEMENTS

We like to thank Proteases and Cancer lab from University of Concepción for supporting this review.

REFERENCES

Ali, M., & Sreekrishnan, T. R. (2001). Aquatic toxicity from pulp and paper mill effluents: a review. Advances in Environmental Research, 5(2), 175–196, https://doi.org/10.1016/S1093-0191(00)00055-1.

Anway, M. D., & Skinner, M. K. (2006). Epigenetic transgenerational actions of endocrine disruptors. Endocrinology, 147(6), s43-s49, https://doi.org/10.1210/en.2005-1058.

Barnes, J. L., Zubair, M., John, K., Poirier, M. C., Martin, F. L. (2018). Carcinogens and DNA damage. Biochemical Society Transactions, 46(5), 1213–1224, https://doi.org/10.1042/BST20180519.

Beischlag, T. V., Luis Morales, J., Hollingshead, B. D., Perdew, G. H. (2008). The aryl hydrocarbon receptor complex and the control of gene expression. Critical reviews in eukaryotic gene expression, 18(3), 207–250, https://doi.org/10.1615/critreveukargeneexpr.v18.i3.20.

Bersten, D. C., Sullivan, A. E., Peet, D. J., Whitelaw, M. L. (2013). bHLH-PAS proteins in cancer. Nature Reviews. Cancer, 13(12), 827–841, https://doi.org/10.1038/nrc3621.

Billiard, S. M., Querbach, K., & Hodson, P. V. (1999). Toxicity of retene to early life stages of two freshwater fish species. Environmental Toxicology and Chemistry: An International Journal, 18(9), 2070-2077, https://doi.org/10.1002/etc.5620180927.

Billiard, S. M., Hahn, M. E., Franks, D. G., Peterson, R. E., Bols, N. C., & Hodson, P. V. (2002). Binding of polycyclic aromatic hydrocarbons (PAHs) to teleost aryl hydrocarbon receptors (AHRs). Comparative biochemistry and physiology part B: biochemistry and molecular biology, 133(1), 55-68, https://doi.org/10.1016/S1096-4959(02)00105-7.

Birkett, J. W., & Lester, J. N. (Eds.). (2002). Endocrine disruptors in wastewater and sludge treatment processes. IWA Publishing.

Buratti, F. M., Volpe, M. T., Meneguz, A., Vittozzi, L., Testai, E. (2003). CYP-specific bioactivation of four organophosphorothioate pesticides by human liver microsomes. Toxicology and Applied Pharmacology, 186(3), 143–154, https://doi.org/10.1016/S0041-008X(02)00027-3.

Camus, P., Solari, M. E. (2008). La invención de la selva austral: Bosques y tierras despejadas en la cuenca del río Valdivia (siglos XVI-XIX). Revista de geografía Norte Grande, (40), 5-22, http://dx.doi.org/10.4067/S0718-34022008000200001.

Casals-Casas, C., & Desvergne, B. (2011). Endocrine disruptors: from endocrine to metabolic disruption. Annual review of physiology, 73, 135-162, https://doi.org/10.1146/annurev-physiol-012110-142200.

Chamorro, S., Hernández, V., Matamoros, V., Domínguez, C., Becerra, J., Vidal, G., Piña, J.M. Bayona. (2013). Chemical characterization of organic microcontaminant sources and biological effects in riverine sediments impacted by urban sewage and pulp mill discharges. Chemosphere, 90(2),611–619, https://doi.org/10.1016/j.chemosphere.2012.08.053.

Chiang, G., Barra, R., Díaz-Jaramillo, M., Rivas, M., Bahamonde, P., Munkittrick, K. R. (2015). Estrogenicity and intersex in juvenile rainbow trout (Oncorhynchus mykiss) exposed to Pine/Eucalyptus pulp and paper production effluent in Chile. Aquatic Toxicology, 164, 126–134, https://doi.org/10.1016/j.aquatox.2015.04.025.

Darbre, P. D. (2017). Endocrine disruptors and obesity. Current obesity reports, 6(1), 18-27, https://doi.org/10.1007/s13679-017-0240-4.

Denissenko, M. F., Pao, A., Tang, M.., Pfeifer, G. P. (1996). Preferential formation of benzo[a]pyrene adducts at lung cancer mutational hotspots in P53. Science, 274(5286), 430–432, https://doi.org/10.1126/science.274.5286.430.

De Oliveira Alves, N., Vessoni, A. T., Quinet, A., Fortunato, R. S., Kajitani, G. S., Peixoto, M. S., & De Medeiros, S. R. B. (2017). Biomass burning in the Amazon region causes DNA damage and cell death in human lung cells. Scientific reports, 7(1), 1-13, https://doi.org/10.1038/s41598-017-11024-3.

Díaz, M. E., Figueroa, R., Alonso, M. L. S., Vidal-Abarca, M. R. (2018). Exploring the complex relations between water resources and social indicators: The Biobío Basin (Chile). Ecosystem Services, 31, 84–92, https://doi.org/10.1016/j.ecoser.2018.03.010.

Diniz, M. S., Peres, I., Castro, L., Freitas, A. C., Rocha-Santos, T. A. P., Pereira, R., & Duarte, A. C. (2010). Impact of a secondary treated bleached Kraft pulp mill effluent in both sexes of goldfish (Carassius auratus L.). Journal of Environmental Science and Health Part A, 45(14), 1858-1865, https://doi.org/10.1080/10934529.2010.520517.

Domenech, T., Bleischwitz, R., Doranova, A., Panayotopoulos, D., & Roman, L. (2019). Mapping Industrial Symbiosis Development in Europe_ typologies of networks, characteristics, performance and contribution to the Circular Economy. Resources, Conservation and Recycling, 141, 76-98, https://doi.org/10.1016/j.resconrec.2018.09.016.

Donoso, P., Otero, L. (2005). Hacia una definición de país forestal: ¿Dónde se sitúa Chile? Bosque (Valdivia), 26(3), http://dx.doi.org/10.4067/S0717-92002005000300002.

Ehrnström-Fuentes, M. (2015). Production of absence through media representation: A case study on legitimacy and deliberation of a pulp mill dispute in southern Chile. Geoforum, 59, 51–62, https://doi.org/10.1016/j.geoforum.2014.11.024.

Ehrnström-Fuentes, M., Kröger, M. (2017). In the shadows of social licence to operate: Untold investment grievances in latin America. Journal of Cleaner Production, 141, 346–358, https://doi.org/10.1016/j.jclepro.2016.09.112.

Essigmann, J. M., Croy, R. G., Nadzan, A. M., Busby, W. F., Reinhold, V. N., Buchi, G., Wogan, G. N. (1977). Structural identification of the major DNA adduct formed by aflatoxin B1 in vitro. Proceedings of the National Academy of Sciences, 74(5), 1870–1874, https://doi.org/10.1073/pnas.74.5.1870.

Estévez, J., Vilanova, E., & Sogorb, M. A. (2019). Biomarkers for testing toxicity and monitoring exposure to xenobiotics. Biomarkers in Toxicology (pp. 1165–1174). Elsevier, https://doi.org/10.1002/jat.769.

Fujii-Kuriyama, Y., Mimura, J. (2005). Molecular mechanisms of AhR functions in the regulation of cytochrome P450 genes. Biochemical and Biophysical Research Communications, 338(1), 311–317, https://doi.org/10.1016/j.bbrc.2005.08.162.

Fujita, S., Chiba, I., Ishizuka, M., Hoshi, H., Iwata, H., Sakakibara, A., Tanabe, S. (2001). P450 in wild animals as a biomarker of environmental impact. Biomarkers: Biochemical Indicators of Exposure, Response, and Susceptibility to Chemicals, 6(1), 19–25, https://doi.org/10.1080/135475001452751.

Gaete, H, Larrain, A., Bay-Schmith, E., Baeza, J., Rodriguez, J. (2000). Ecotoxicological assessment of two pulp mill effluent, biobio river basin, chile. Bulletin of environmental contamination and toxicology, 65(2), 183–189, https://doi.org/10.1007/s0012800113.

Gaete, Hernán, Paredes, K. (1996). Toxicidad de mezclas de contaminantes químicos sobre el cladócero Daphnia magna. Revista Internacional de Contaminación Ambiental, 12(1), 23-28

Gelboin, H. V. (1980). Benzo [alpha] pyrene metabolism, activation and carcinogenesis: role and regulation of mixed-function oxidases and related enzymes. Physiological reviews, 60(4), 1107-1166, https://doi.org/10.1152/physrev.1980.60.4.1107.

Gysling, A. J., Álvarez, V. D. C., Soto, D. A., Pardo, E. J., Poblete, P. A., & Khaler, C. (2019). Anuario Forestal 2019 [Chilean Statistical Yearbook of Forestry 2019]. Instituto Forestal [Forestry Institute], Santiago, Chile.

Hawliczek, A., Nota, B., Cenijn, P., Kamstra, J., Pieterse, B., Winter, R., & Legler, J. (2012). Developmental toxicity and endocrine disrupting potency of 4-azapyrene, benzo [b] fluorene and retene in the zebrafish Danio rerio. Reproductive toxicology, 33(2), 213-223, https://doi.org/10.1016/j.reprotox.2011.11.001.

Hecht, S. S. (1999). DNA adduct formation from tobacco-specific N-nitrosamines. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis, 424(1–2), 127–142, https://doi.org/10.1016/S0027-5107(99)00014-7.

Hernández, V., Eberlin, M. N., Chamorro, S., Becerra, J., Silva, M. (2013). Steroidal metabolites in Chilean river sediments influenced by pulp mill effluents. Journal of the Chilean Chemical Society, 58(4), 2035–2037, http://dx.doi.org/10.4067/S0717-97072013000400029.

Hong, J. Y., Yang, C. S. (1997). Genetic polymorphism of cytochrome P450 as a biomarker of susceptibility to environmental toxicity. Environmental Health Perspectives, 105 Suppl 4, 759–762, https://doi.org/10.1289/ehp.97105s4759.

Huang, M., Mesaros, C., Hackfeld, L. C., Hodge, R. P., Zang, T., Blair, I. A., & Penning, T. M. (2017). Potential metabolic activation of a representative C4-alkylated polycyclic aromatic hydrocarbon retene (1-methyl-7-isopropyl-phenanthrene) associated with the deepwater horizon oil spill in human hepatoma (HepG2) cells. Chemical research in toxicology, 30(4), 1093-1101, https://doi.org/10.1021/acs.chemrestox.6b00457.

Jansen van Rensburg, G., Bervoets, L., Smit, N. J., Wepener, V., van Vuren, J. (2019). Biomarker Responses in the Freshwater Shrimp Caridina nilotica as Indicators of Persistent Pollutant Exposure. Bulletin of environmental contamination and toxicology, https://doi.org/10.1007/s00128-019-02773-0.

Jarvis, I. W., Dreij, K., Mattsson, Å., Jernström, B., & Stenius, U. (2014). Interactions between polycyclic aromatic hydrocarbons in complex mixtures and implications for cancer risk assessment. Toxicology, 321, 27-39, https://doi.org/10.1016/j.tox.2014.03.012.

Lahdelma, I., & Oikari, A. (2005). Resin Acids and Retene in Sediments Adjacent to Pulp and Paper Industries (8 pp). Journal of Soils and Sediments, 5(2), 74-81, https://doi.org/10.1065/jss2005.05.139.

Li, S., Pei, X., Zhang, W., Xie, H. Q., & Zhao, B. (2014). Functional analysis of the dioxin response elements (DREs) of the murine CYP1A1 gene promoter: beyond the core DRE sequence. International journal of molecular sciences, 15(4), 6475-6487.

Marchand-Geneste, N., & Carpy, A. (2003). Theoretical study of the thermal degradation pathways of abietane skeleton diterpenoids: Aromatization to retene. Journal of Molecular Structure: THEOCHEM, 635(1-3), 55-82., https://doi.org/10.1016/S0166-1280(03)00401-9.

Massion, P. P., Sequist, L. V., Pao, W. (2016). Biology of lung cancer. Murray and Nadel's textbook of respiratory medicine (pp. 912-926.e6). Elsevier, https://doi.org/10.1016/B978-1-4557-3383-5.00051-8.

Ministerio de Obras públicas.(1998). Establece norma de emisión para la regulación de contaminantes asociados a las descargas de residuos industriales líquidos a sistemas de alcantarillado. Decreto Supremo 609. Diario oficial de la república de Chile. Chile.

Ministerio secretaría general de la presidencia. (2001). Establece norma de emisión para la regulación de contaminantes asociados a las descargas de residuos líquidos a aguas marinas y continentales superficiales. Decreto supremo 90. Diario oficial de la república de Chile. Chile

Ministerio de Salud.(2003). Aprueba reglamento sanitario sobre manejo de residuos peligrosos. Decreto supremo 148. Diario oficial de la república de Chile. Chile.

Ministerio de Salud de Chile. (2011). Departamento de Estadísticas e Información en Salud. Indicadores Básicos de Salud Chile

Murray, I. A., Patterson, A. D., Perdew, G. H. (2014). Aryl hydrocarbon receptor ligands in cancer: friend and foe. Nature Reviews. Cancer, 14(12), 801–814, https://doi.org/10.1038/nrc3846.

Molina-Sánchez, E., Leyva-Díaz, J. C., Cortés-García, F. J., & Molina-Moreno, V. (2018). Proposal of sustainability indicators for the waste management from the paper industry within the circular economy model. Water, 10(8), 1014, https://doi.org/10.3390/w10081014.

Oikari, A., Fragoso, N., Leppänen, H., Chan, T., & Hodson, P. V. (2002). Bioavailability to juvenile rainbow trout (Oncorhynchus mykiss) of retene and other mixed-function oxygenase-active compounds from sediments. Environmental Toxicology and Chemistry: An International Journal, 21(1), 121-128, https://doi.org/10.1002/etc.5620210118.

Orrego, R., Burgos, A., Moraga-Cid, G., Inzunza, B., Gonzalez, M., Valenzuela, A., Barra, R.(2006). Effects of pulp and paper mill discharges on caged rainbow trout (Oncorhynchus mykiss): biomarker responses along a pollution gradient in the Biobio River, Chile. Environmental Toxicology and Chemistry, 25(9), 2280–2287, https://doi.org/10.1897/05-385R.1.

Pacto Global.(2015). Reciclaje en Chile: Las cifras en Chile.Pacto Global ONU. https://pactoglobal.cl/2015/el-reciclaje-las-cifras-en-chile/.

Plant, A. L., Knapp, R. D., & Smith, L. C. (1987). Mechanism and rate of permeation of cells by polycyclic aromatic hydrocarbons. Journal of Biological Chemistry, 262(6), 2514-2519, https://doi.org/10.1016/S0021-9258(18)61534-0.

Peixoto, M. S., da Silva Junior, F. C., de Oliveira Galvão, M. F., Roubicek, D. A., de Oliveira Alves, N., & de Medeiros, S. R. B. (2019). Oxidative stress, mutagenic effects, and cell death induced by retene. Chemosphere, 231, 518-527, https://doi.org/10.1016/j.chemosphere.2019.05.123.

Potting, J., Hekkert, M. P., Worrell, E., & Hanemaaijer, A. (2017). Circular economy: measuring innovation in the product chain (No. 2544). PBL Publishers.

Poirier, M. C. (2016). Linking DNA adduct formation and human cancer risk in chemical carcinogenesis. Environmental and molecular mutagenesis, 57(7), 499-507, https://doi.org/10.1002/em.22030.

Räsänen, K., Arsiola, T., Oikari, A. (2012). Fast genomic biomarker responses of retene and pyrene in liver of juvenile rainbow trout, Oncorhynchus mykiss. Bulletin of environmental contamination and toxicology, 89(4), 733–738, https://doi.org/10.1007/s00128-012-0770-0.

Ramdahl, T. (1983). Retene—a molecular marker of wood combustion in ambient air. Nature, 306(5943), 580-582, https://doi.org/10.1038/306580a0.

Regnault, C., Usal, M., Veyrenc, S., Couturier, K., Batandier, C., Bulteau, A. L., Le May, C. (2018). Unexpected metabolic disorders induced by endocrine disruptors in Xenopus tropicalis provide new lead for understanding amphibian decline. Proceedings of the National Academy of Sciences, 115(19), E4416-E4425, https://doi.org/10.1073/pnas.1721267115.

Rigol, A., Latorre, A., Lacorte, S., & Barceló, D. (2002). Determination of toxic compounds in paper-recycling process waters by gas chromatography–mass spectrometry and liquid chromatography–mass spectrometry. Journal of Chromatography A, 963(1-2), 265-275, https://doi.org/10.1016/S0021-9673(02)00232-7.

Salas, C., Donoso, P. J., Vargas, R., Arriagada, C. A., Pedraza, R., Soto, D. P. (2016). The forest sector in chile: an overview and current challenges. Journal of Forestry, 114(5), 562–571, https://doi.org/10.5849/jof.14-062.

Simão, L., Hotza, D., Raupp-Pereira, F., Labrincha, J. A., Montedo, O. R. K. (2018). Wastes from pulp and paper mills - a review of generation and recycling alternatives. Cerâmica, 64(371), 443–453, https://doi.org/10.1590/0366-69132018643712414.

Simoneit, B. R. (2002). Biomass burning—a review of organic tracers for smoke from incomplete combustion. Applied Geochemistry, 17(3), 129-162, https://doi.org/10.1016/S0883-2927(01)00061-0.

Singh, A. K., Chandra, R. (2019). Pollutants released from the pulp paper industry: Aquatic toxicity and their health hazards. Aquatic Toxicology, 211, 202–216, https://doi.org/10.1016/j.aquatox.2019.04.007.

Szeliga, J., & Dipple, A. (1998). DNA adduct formation by polycyclic aromatic hydrocarbon dihydrodiol epoxides. Chemical research in toxicology, 11(1), 1-11, https://doi.org/10.1021/tx970142f.

Takano, H., Yanagisawa, R., Ichinose, T., Sadakane, K., Inoue, K., Yoshida, S., Takeda, K.(2002). Lung expression of cytochrome P450 1A1 as a possible biomarker of exposure to diesel exhaust particles. Archives of Toxicology, 76(3), 146–151, https://doi.org/10.1007/s00204-002-0323-0.

Tarantini, A., Maître, A., Lefèbvre, E., Marques, M., Rajhi, A., Douki, T. (2011). Polycyclic aromatic hydrocarbons in binary mixtures modulate the efficiency of benzo[a]pyrene to form DNA adducts in human cells. Toxicology, 279(1–3), 36–44, https://doi.org/10.1016/j.tox.2010.09.002.

Terasaki, M., Fukazawa, H., Tani, Y., & Makino, M. (2008). Organic pollutants in paper-recycling process water discharge areas: First detection and emission in aquatic environment. Environmental Pollution, 151(1), 53-59, https://doi.org/10.1016/j.envpol.2007.03.012.

Top, E. M., Springael, D. (2003). The role of mobile genetic elements in bacterial adaptation to xenobiotic organic compounds. Current Opinion in Biotechnology, 14(3), 262–269, https://doi.org/10.1016/S0958-1669(03)00066-1.

Uğurlu, M., Gürses, A., Doğar, C., Yalçın, M. (2008). The removal of lignin and phenol from paper mill effluents by electrocoagulation. Journal of Environmental Management, 87(3), 420–428, https://doi.org/10.1016/j.jenvman.2007.01.007.