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Article

Estimating the Carcinogenic Risks of Major Pollutants Released into the Environment

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SUMMARY

Each year, large amounts of carcinogenic pollutants are released into the environment, which negatively affects human health. This study ranks the major carcinogenic pollutants that are released into the air, water, and land by both the total released amounts and the potential carcinogenic risks. We hypothesized that the carcinogenic pollutants released in the greatest quantities have the highest carcinogenic risks to human beings. Based on the available data and our preliminary analysis, the carcinogenic pollutants that are released the most include the air pollutants styrene and acetaldehyde, the water pollutants acetaldehyde and formaldehyde, as well as the land pollutants asbestos (friable) and nickel compounds. The pollutants with the highest carcinogenic risks, estimated by the total released carcinogenic doses, include formaldehyde and styrene released into the air, cadmium and formaldehyde released into water, and cadmium and cobalt compounds released into the land. The results suggest that the pollutants with the highest carcinogenic risks may not necessarily be the ones released in the greatest quantities into the environment due to different carcinogenic potency of the pollutants. This study could help to promote public awareness of the potential carcinogenic risks of environmental pollutants and help policy makers to focus on the high-risk items.

INTRODUCTION

Every year, large amounts of toxic waste are released to the air, water, and land, polluting our living environment. The toxic substances are absorbed into our bodies through inhalation, ingestion, or the skin, and cause health problems (1). The global waste crisis is becoming a major environmental and health issue in our age.

Carcinogens are materials that can cause cancer to humans through mechanisms such as irreversible genetic damage or mutations. Carcinogenic chemicals are classified by the International Agency for Research on Cancer (IARC), the National Toxicology Program (NTP), or 29 CFR Part 1910 Subpart Z as known or probable carcinogens (2). Known carcinogens include benzene, asbestos, cadmium, nickel, arsenic and their compounds, formaldehyde, etc. Carcinogenic pollutants are released not only by industries, but also by household waste. Many of today's household products such as televisions, computers, and phones contain toxic chemicals that can pollute the air and contaminate soil and water. Every year, over two million tons of carcinogens are released to the environment. Scientists estimated that over 10,000 deaths each year may be attributable to the exposure to carcinogens released to the environment (3). For example, while smoking is the most common cause for lung cancers, 10–15% of lung cancer cases worldwide are lifetime nonsmokers (4). Environmental exposure to carcinogens such as arsenic, asbestos, radon, and polluted air may be the cause for nonsmokers developing lung cancer. Due to the complexity of environmental conditions, health status, and social activities, it is difficult to study how environmental exposure leads to cancer development.

Established under the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) and Pollution Prevention Act of 1990, the Toxics Release Inventory (TRI) managed by the Environmental Protection Agency (EPA) is a publicly available database with toxic chemical release information in the United States (5). Manufacturing facilities that produce more than 25,000 pounds annually or use more than 10,000 pounds of listed toxic chemicals annually are required to report it to the TRI. The TRI database is available online with annual chemical release data from 1987.

The potency of a carcinogen is estimated by the medium toxic dose (TD_{50}) in rats and mice. TD_{50} is the chronic dose-rate in mg/kg body wt/day that would induce tumors in 50% of the test animals at the end of a standard lifespan (6). The Carcinogen Potency Database (CPDB) is a publicly available database reporting carcinogenic potency of 1547 chemicals based on 6540 chronic, long-term animal cancer tests from 1980 to 2011 (6). It was developed by the Carcinogenic Potency Project at the University of California, Berkeley and the Lawrence Berkeley National Laboratory. Currently the information is searchable through the website www.toxinfo.io/.

Most environmental pollutants play important roles in the initiation, promotion, and progression of cancer cells through various mechanisms such as DNA damage, signal transduction interference, oxidation, and enzyme inhibition **(Figure 1)** (7). The negative effects of environmental pollutants on human health are well documented. Numerous studies have revealed elevated risk ratios of different cancers in organs such as stomach, prostate, liver, lung, and women's breast and cervix among residents living near waste landfill sites (8–13) or industrial plants (14–16). Increased cancer risks are also associated with water contaminated with carcinogens such as chromium (17), arsenic (18), atrazine, and nitrate (19). Similarly, the higher prevalence of lung cancer in urban areas is associated with the presence of carcinogens in urban air (4, 20–22).

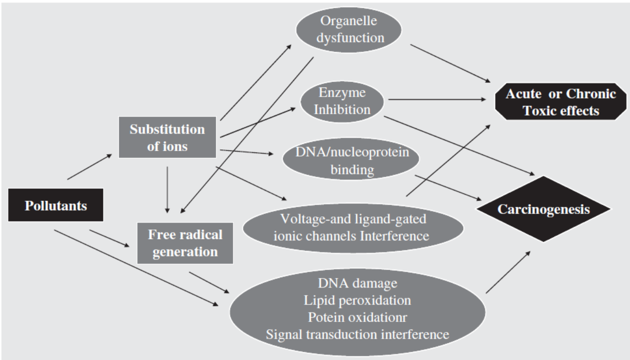

Figure 1: Basic Mechanism of Carcinogenesis. This schematic diagram illustrates the effects of pollutants on carcinogenesis, adapted from *Kampa and Castanas. "Human Health Effects of Air Pollution." doi:10.1016/j.envpol.2007.06.012*. Most environmental pollutants play important roles in the initiation, promotion, and progression of cancer cells through various mechanisms such as DNA damage, signal transduction interference, oxidation, and enzyme inhibition.

The purpose of this study was to rank the major carcinogenic pollutants that are released into the air, water, and land by both the total released amounts and the potential carcinogenic risks. We hypothesized that the most released carcinogenic pollutants have the highest carcinogenic risks to human beings. The carcinogenic risks are estimated based on the total carcinogenic doses, which are calculated by dividing the total released amount of the pollutant by the measured TD_{50} in rats or mice. We used the Pareto charts to illustrate the rank of the total released amounts of carcinogens and the total carcinogenic doses released into the air, water, and land in the United States in 2018 (5). The results of this study can help promote public awareness of the potential carcinogenic risks of pollutants and help policy makers identify the high-risk pollutants so that this information can be used in policy making.

RESULTS

Carcinogens Released into the Air

We used Pareto charts to display the top carcinogenic pollutants released into the air **(Figure 2).** Based on the total amounts of pollutants released into the air (5), the top three pollutants released in the greatest quantities are styrene (13,042 metric tons), acetaldehyde (3,762 metric tons), and formaldehyde (2,089 metric tons) **(Figure 2A)**. Pareto charts illustrate the total released carcinogenic doses, calculated based on the total release amounts into air and rat and mouse TD_{50} values, respectively **(Figure 2B and 2C)**. Based on the rat TD_{50} data, the pollutant with the highest total carcinogenic doses released into air was formaldehyde, with a total of 1.5 x 10^{12} rat doses, which was almost three-fold greater than styrene (a total of 5.6 x 10^{11} rat doses), though styrene is released in the greatest quantities into the air (Figure 2B). Though released less in amount than styrene and acetaldehyde, formaldehyde is a more potent carcinogen, with a reported rat TD_{50} value of 1.35 mg/kg/day, which is the lowest among air pollutants. Acetaldehyde, on the other hand, has much less carcinogenic risk, with a total of only 2.4 x 10^{10} rat doses. Based on mouse TD_{50} values, however, styrene still releases the most carcinogenic doses among the air pollutants, with a total of 6.2 x 10^{10} mouse doses, which is only slightly more than formaldehyde (a total of 4.7 x 10^{10} mouse doses) **(Figure 2C)**. Mouse TD_{50} was not reported for acetaldehyde in the CPDB database.

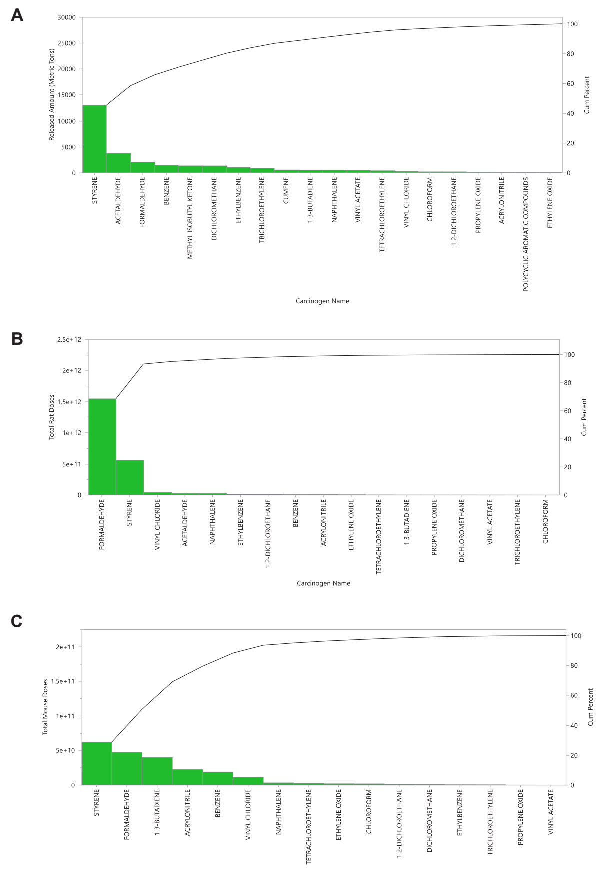

Figure 2: Major Carcinogenic Pollutants Released into the Air. The Pareto charts illustrate the top carcinogenic pollutants released into the air by total released amounts (A), total carcinogenic doses based on rat (B) and mouse (C) toxicology studies. The bars represent the released amounts in metric tons (A) and carcinogenic risk in total rat doses (B) or total mouse doses (C), with scales on the left Y axis. The lines above the bars represent the cumulative percentage, with scales on the right.

Carcinogens Released into Water

We used Pareto charts to illustrate the top carcinogen pollutants released into water **(Figure 3)**. Based on the total amount of pollutants released into water (5), the top three pollutants released in the greatest quantities are acetaldehyde (170 metric tons), formaldehyde (97 metric tons), and 1,4-dioxane (45 metric tons) **(Figure 3A)**. Pareto charts illustrate the calculated total released carcinogenic doses, calculated based on the total release amounts into water and rat and mouse TD_{50} values (6), respectively **(Figure 3B and 3C).** The pollutants that have the highest carcinogenic dose released into water are cadmium compounds, with a total of 6.4 x 10^{11} rat doses **(Figure 3B),** and formaldehyde, with totals of 7.2 x 10^{10} rat doses **(Figure 3B)** and 2.2 x 10^{9} mouse doses **(Figure 3C)**, respectively. The dose of cadmium compounds was estimated by using the reported TD_{50} of soluble salt cadmium chloride, 0.0136 mg/kg/day, which is the lowest among the water pollutants (6). Again, though released in smaller amounts than acetaldehyde, formaldehyde is a more potent carcinogen.

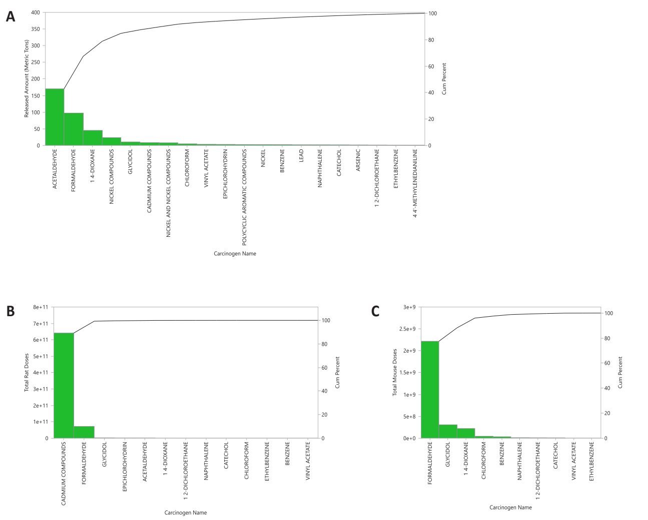

Figure 3: Major Carcinogenic Pollutants Released into Water
The Pareto charts illustrate the top carcinogenic pollutants released into water by total released amounts (A), total carcinogenic doses based on rat (B) and mouse (C) toxicology studies. The bars represent the released amounts in metric tons (A) and carcinogenic risk in total rat doses (B) or total mouse doses (C), with scales on the left Y axis. The lines above the bars represent the cumulative percentage, with scales on the right Y axis.

Carcinogens Released to Land

Pareto charts illustrate the major carcinogenic pollutants released to land **(Figure 4)**. Based on the total amount of pollutants released to land (5), the three land pollutants released in the largest amounts are asbestos (friable) (13,992 metric tons), nickel and nickel compounds (6,195 metric tons), and nickel compounds (4,932 metric tons) **(Figure 4A)**. The TRI database lists nickel and nickel compounds and nickel compounds separately (the same for some other heavy metal pollutants), we illustrated them as separate pollutants in the charts for convenience and addressed this in the Discussion Section. Many of the pollutants, including asbestos (friable), nickel and nickel compounds, and nickel compounds, were not tested, thus no TD_{50} values are available. Based on the pollutants with available TD_{50} values, the top pollutants that have the highest carcinogenic dose released to land are cadmium compounds, cadmium and cadmium compounds, and cadmium, with totals of 1.2 x 10^{14}, 4.0 x 10^{13}, and 1.1 x 10^{13} rat doses, respectively **(Figure 4B).** Based on the measured TD_{50} data in mice, cobalt has a total released dose of 1.5 x 10^{11} mouse doses **(Figure 4C)**. The doses of cadmium and cobalt and their compounds were estimated by using the available TD_{50} data of soluble salts cadmium chloride and cobalt sulfate. Note that TD_{50} data of many land pollutants are missing and not illustrated in the charts.

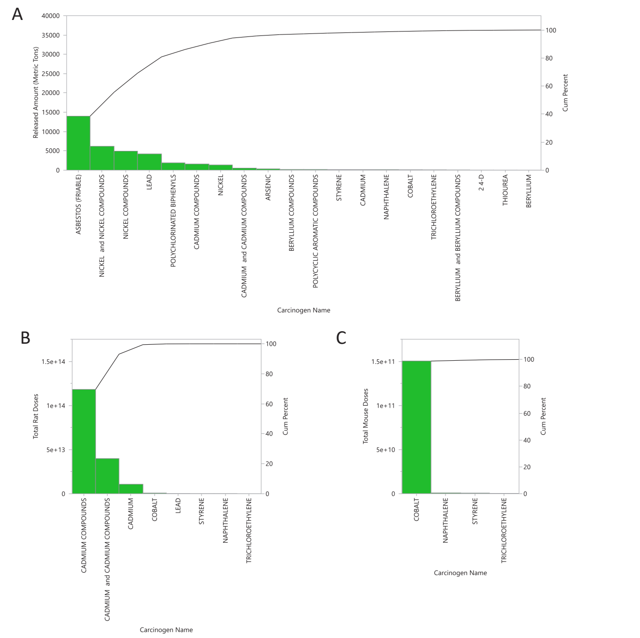

Figure 4: Major Carcinogenic Pollutants Released to Land
The Pareto charts illustrate the major carcinogenic pollutants released to land by total released amounts (A), total carcinogenic doses based on rat (B) and mouse (C) toxicology studies. The bars represent the released amounts in metric tons (A) and the carcinogenic risk in total rat doses (B) or total mouse doses (C), with scales on the left Y axis. The lines above the bars represent the cumulative percentage, with scales on the right Y axis. Note that TD_{50} data of many land pollutants are missing and not illustrated in the charts.

DISCUSSION

This study ranked the major carcinogenic pollutants that are released to air, water, and land by both the total released amounts and the total released carcinogenic doses. We hypothesized that the most released carcinogenic pollutants have the highest potential carcinogenic risks. The carcinogenic risks were estimated based on the total carcinogenic doses calculated by dividing the total released amount in the United States in 2018 (5) by the measured TD_{50} in rats or mice (6). We used Pareto charts to illustrate the major carcinogenic pollutants released to the environment based on both the released amounts and the total released carcinogenic doses. Based on the available data, the pollutants with the highest potential carcinogenic risks are not necessarily the ones that are released the most to the environment, due to the different carcinogenic potency of the pollutants. The high carcinogenic risks come from the pollutants such as formaldehyde and styrene released to air, cadmium and formaldehyde released to water, and cadmium and cobalt compounds released to land.

The total released amounts of carcinogens were obtained by searching the TRI database (4). Due to time and resource limitations, we only focused on the top 20 carcinogenic pollutants that were released the most to air, water, and land for comparison. The TD_{50}, a measure of carcinogenic potency, was reported based on studies in rats and mice between 1980 to 2011, compiled in the Carcinogen Potency Database (CPDB) (6). Currently CPDB is located at https://www.toxinfo.io/. Though it is still searchable and retains records for the years 1980 to 2011, this database is no longer updated. It is important to consider that the carcinogenic potency, TD_{50}, varies between different species. For example, the reported rat TD_{50} of formaldehyde is 1.35 mg/kg/day, which is the lowest among air pollutants. However, the mouse TD_{50} of formaldehyde is 43.9 mg/kg/day, much higher than the TD_{50} of acrylonitrile (6.32 mg/kg/day), 1,3-butadiene (13.9 mg/kg/day), and vinyl chloride (21.8 mg/kg/day). Thus, the carcinogenic risk estimated based on experimental animals may be different than the potential risk to humans. In addition, the TD_{50} values for many carcinogens, including some of the most released pollutants, such as asbestos (friable) and nickel, were unavailable from the CPDB. Furthermore, there are inconsistencies in nomenclature for some of the pollutants reported in the TRI database, and some pollutants are not well defined (5). For example, cadmium, cadmium compounds, and cadmium and cadmium compounds are reported in parallel in the TRI database, as are nickel and cobalt compounds. Also, polycyclic aromatic compounds represent a group of molecules that was reported in TRI in parallel with individual molecules. These factors added complexity to our evaluation process. For estimation purposes, in the cases of some compounds such as cadmium, cobalt, and their compounds, the TD_{50} values of their soluble salts, cadmium chloride and cobalt sulfate, were used for risk estimation. Thus, due to all the reasons stated above, the results reported in this study should be considered preliminary and should be used with caution. Nevertheless, our results are consistent with the fact that formaldehyde, classified as "known to be a human carcinogen" by the National Toxicology Program (NTP), is the most important carcinogen among the 187 air pollutants identified by the U.S. EPA, and scientists estimated that between 6,600–12,500 people in the U.S. develop cancer over their lifetimes from exposure to air polluted with formaldehyde (23). NTP classifies cadmium and cadmium compounds as "known to be a human carcinogen" (24), and cobalt and cobalt compounds, as "reasonably anticipated to be human carcinogen" (25). To estimate the carcinogenic risks, the reported TD_{50} values of the soluble salts of cadmium and cobalt, cadmium chloride and cobalt sulfate, were used. Cadmium chloride has a rat TD_{50} of 0.0136 mg/kg/day, and no data for mouse TD_{50}. Cobalt sulfate has a rat TD_{50} of 0.137 mg/kg/day and a mouse TD_{50} of 0.756 mg/kg/day, respectively. These pollutants are potent carcinogens in experimental animals.

In summary, we used Pareto charts to identify the major carcinogenic pollutants released to the environment based on both the released amounts and the total released carcinogenic doses, based on the available data searched from the TRI and CPDB databases. The top pollutants with the highest potential carcinogenic risks are not necessarily the ones that are released the most to the environment, due to the different carcinogenic potency of the pollutants. Further studies focus on the top ranked carcinogen pollutants are needed to understand their effects on the environment and human carcinogenesis. This study could help to promote public awareness of the potential carcinogenic risks of environmental pollutants and help policy makers to focus on the most high-risk pollutants when designing policies.

MATERIALS AND METHODS

The amounts of carcinogen pollutants released to air, water, and land were obtained by searching the Toxic Release Inventory (TRI) database at the Envirofacts website of U.S. Environmental Protection Agency (EPA) (website: https://www.epa.gov/enviro/tri-ez-search), using the TRI EZ Search with the following search criteria: 1) Chemical Released to Air, Water, or Land; 2) Reporting Year – 2018; 3) Chemical Name – leave open; 4) Carcinogen Chemical Indicator – Y (yes); and 5) Total Release – Sum (5). The top 20 carcinogenic pollutants released the most to air, water, and land were included for evaluation in this study.

The carcinogenic potency, TD_{50}, of a carcinogen was based on the data reported by the Carcinogen Potency Database (CPDB), based on data from rat and mouse studies between 1980 and 2011 (6). The TD_{50} data are currently searchable at the website https://www.toxinfo.io/ by inputting the chemical name and searching under CPDB; however, the TD_{50} data are no longer updated. The TD_{50} is a quantitative estimation of chronic dose-rate in mg/kg body wt/day which would induce tumors in half the test animals at the end of a standard lifespan for the species. For a detailed definition of TD_{50} and the statistical methods for estimating TD_{50}, refer to Carcinogenic Potency (TD_{50}) (6). A low TD_{50} value indicates a potent carcinogen, whereas a high value indicates a weak one.

The carcinogenic risk of released pollutants was estimated by the total dose released to the environment, which was calculated by dividing the total released amount by the reported TD_{50} in rat or mouse studies (6), according to the following equation:

$$Total\ Carcinogenic\ Dose = \frac{Total\ Amount\ Released\ (mg)}{TD_{50}\ (mg/kg/Day)}$$

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