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Cadmium-contaminated jambu: Carcinogenic and non-carcinogenic risks to human health

Jambu contaminado com cádmio: Riscos carcinogênicos e não carcinogênicos à saúde humana

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RESUMO

Conforme o desenvolvimento das indústrias e o crescimento populacional de forma exponencial, o consumo de produtos e a produção aumentaram a geração de resíduos liberados no meio ambiente. Esses resíduos liberados advindas principalmente de indústrias de processamento e o uso de fertilizantes a base de fosfato são acompanhadas de elementos-traço. Esses elementos-traço podem contaminar solos utilizados para cultivo de hortaliças. Nessa perspectiva, o jambu chama atenção devido ao fato de ser uma planta que pode se desenvolver em ambiente contaminado com cádmio. A sua capacidade de acumular o Cd e a constante expansão de atividades industriais para as redondezas de áreas de cultivo, podem expor a população ao risco. Com isso, a seguinte pesquisa usou equações de risco carcinogênicos e não carcinogênicos para estimar os valores de risco. Foi estudado três partes comestíveis do jambu (caule, folha e flor) contaminadas com cádmio e objetivou-se responder se o jambu contaminado realmente oferece risco a população, quais doses mais oferecem risco carcinogênico ou não carcinogênico e quais os possíveis riscos infligidos ao ser humano.

Palavras-chave: Efeitos adversos; Metais pesados; saúde humana

ABSTRACT

As industries develop and population grows exponentially, product consumption and production increase the generation of waste released into the environment. These residues released mainly from processing industries and the use of phosphate-based fertilizers are accompanied by trace elements. These trace elements can contaminate soils used to grow vegetables. From this perspective, jambu attracts attention due to the fact that it is a plant that can grow in an environment contaminated with cadmium. Its ability to accumulate Cd and the constant expansion of industrial activities to the vicinity of cultivation areas can expose the population to risk. Therefore, the following research used carcinogenic and non-carcinogenic risk equations to estimate risk values. Three edible parts of jambu (stem, leaf and flower) contaminated with cadmium were studied and the objective was to answer whether contaminated jambu really poses a risk to the population, which doses most pose a carcinogenic or non-carcinogenic risk and what are the possible risks inflicted on humans.

Keywords: Adverse effects; Heavy metals; human health.

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INTRODUCTION

As the growth of industrial production processes, population and, consequently, the consumption of many types of products has increased, negative environmental impacts have worsened over the years (CRIST et al., 2017).

Due to this growth in both production and population, the contaminant residues released into the environment have increased exponentially, trace elements in particular. The current soils present trace elements from several sources, being them from lithogenic and pedogenic processes (being of lithogenic origin, however, having its dynamics changed by pedogenic processes) and anthropogenic factors, direct or indirect results of human action (KABATA-PENDIAS, 2011).

The release of trace elements directly affects the soil. Soils in the vicinity of industrial areas can have various groups of metals, which will depend on the activity developed at the site. Regarding soils in urban areas, they are usually contaminated with lead, zinc, cadmium, and copper, derived from vehicle traffic, paints, and other sources (ALLOWAY, 2013).

Trace element contamination of soil, water, and air can affect human health directly and indirectly through food consumption (GLAVAC et al.. 2017). Pointing out that high levels of heavy metals in living tissues can cause severe organ impairment, neurological disorders, and eventually death (ABDU et al., 2016).

Trace elements can be found in nature mainly because of anthropogenic activities such as mining, smelting industries, and refineries, as well as in products such as plastics, pigments, and ceramics. These activities generate an exacerbated increase in the concentration of trace elements in the environment (HAYAT et al., 2019). Due to this process, concerns are growing about food insecurity in view of soil pollution.

One of the most researched trace elements from the point of view of food safety is cadmium (Cd), because its origin in the environment through supergene geological processes, such as weathering and erosion of minerals containing the element enable its presence in the environment. However, one of the main sources to the environment is the intensive use of phosphate fertilizers, use of sewage sludge in agriculture and application of pesticides based on trace elements (ALLOWAY, 2013, OLIVEIRA et al., 2022a; OLIVEIRA et al 2022b).

The presence of cadmium can lead to serious health problems, and the ability of plants to accumulate these elements carry these contaminants into the human food chain (ALADESANMI, et al 2019).

By accumulating in plants and animals, cadmium (Cd) generates concern about its toxicity levels, considering that the exposure to the element occurs primarily through the ingestion of contaminated food and water, and can lead to the emergence of several types of cancer, such as breast, lung, prostate, pancreas and nasopharynx cancer (GENCHI, et al. 2020). When consumed by humans in a prolonged manner, cadmium can lead to deleterious health effects, such as prostate proliferative lesions, kidney damage, bone problems, lung cancer, hypertension among other effects (MOHAMMADI, et al. 2019).

In this context, the presence of cadmium in soils generates concern about the contamination of the population through the consumption of plants that bioaccumulate the element, such as Acmella oleracea (jambu), given that it grows even in an environment contaminated with high doses of cadmium, being tolerant and bioaccumulator of the metal (HUNGRIA et al., 2019; OLIVEIRA et al., 2022a; OLIVEIRA et al., 2022b).

Therefore, the importance of this study, based on the fact of the increasingly wide consumption of jambu around the world and its continuous consumption by the population, mostly in the northern region of the country. Due to the bioaccumulative property of jambu and the toxicity of cadmium, it is important to investigate the possible carcinogenic and noncarcinogenic effects on human health.

MATERIALS AND METHODS

Estimated daily consumption of heavy metals

Several authors have already spelled out in their papers equations to estimate the daily intake of trace elements by people (HU *et al*, 2017; ZHONG et *al*, 2018; CHEN *et al*, 2018a). Therefore, the following research used data from an experiment in hydroponic growing system, where jambu was contaminated with increasing doses of cadmium (1, 3, 6 and 9 $mg.kg^{-1}$) in the form of cadmium chloride ($CdCl_2$). The pots used for growing jambu were filled with pre-washed ground silica and lined with aluminum foil to avoid solar incidence. The nutrient solution used was thatof Hoagland and Arnon (1950) and the pots were perforated at the base, with the introduction of a silicone tube to facilitate the recirculation of the nutrient solution. Everyseven days the cadmium doses were renewed, along with the nutrient solution. From the data generated by the biometric analysis of the aforementioned experiment, a calculationwas made for each edible part of the jambu (leaf, stem, and flower) to estimatethe carcinogenic and non-carcinogenic risks.

To estimate the estimated daily consumption (EDC), the following equation was used:

$$\text{EDC} = C \; x \; \text{ADC} \; x \; \text{EF} \; x \; \text{ED} \,/\, \text{BW} \; x \; \text{AT} \; x \; 0{,}001 \quad (1)$$

where C ($mg.kg^{-1}$) is the metal concentration in jambu, ADC ($g.person^{-1}.day^{-1}$) is the average daily consumption of jambu, EF is the exposure frequency (365 $days.year^{-1}$), ED is the exposure duration (70 years, according to the average lifespan), DW is the bodyweight ($kg.person^{-1}$) and AT is the average time (365 $days.year^{-1}$ x years of exposure, considered 70 years in the present study) (SATPATHY *et al*, 2014).

The estimated daily consumption is used to estimate how much of a certain plant a person consumes, where an average consumption value is obtained and used to calculate the other variables.

Target Risk Quotient

As presented by (MOKARRAM et al, 2021; ILECHUKWU et al, 2021), the Target Risk Quotient (TRQ) is used to estimate the non-carcinogenic risks to human health from consuming leafy vegetables contaminated with heavy metals. The TRQ was calculated according to equation 2:

$$\text{TRQ} = \text{EDC}/\text{ODF} \quad (2)$$

where EDC is the estimated daily consumptiom in $mg.day^{-1}.kg^{-1}$ of body weight and ODF is the oral dose of reference (GEBEYEHU and BAYISSA, 2020) with the oral dose reference value being 0.001. It is considered that there is no potential risk when TRQ < 1 (REHMAN et al, 2016). This value indicates the possible diseases that humans can develop that are not carcinogenic.

Carcinogenic Risk

To calculate the carcinogenic risk (CR), the following equation was used;

$$\text{CR} = \text{EDC} \; x \; \text{CSF} \quad (3)$$

where EDC is the estimated daily consumption in $mg.day^{-1}.kg^{-1}$ and CSF is the cancer slope factor ($mg.day^{-1}.kg^{-1}$). A value of 1 x 10-6 is considered as the risk threshold (GEBEYEHU and BAYISSA, 2020). It is worth noting that the value of the Cancer Slope Factor for cadmium was found to be 0.38, according to Yang et al, (2018).

The carcinogenic risk value indicates the possibility of a person developing any type of cancer as a result of prolonged consumption of trace elements. This consumption occurs orally through previously contaminated food.

Three edible parts of the plant were considered for the calculations, being leaf, stem, and inflorescence, respectively. The distribution of the metal and the capacity of the plant to bioaccumulate varies in the system, influencing different values of accumulated metal for different parts of the plant.

The data for all parts of the plant studied used as human consumption limit 100 grams per day of jambu. From these data, the averages were taken to obtain the standard deviation for each treatment. Regression analysis was done to visualize which dose of each treatment has the greatest statistical relevance and consequently the greatest potential for harm.

The data were submitted to regression analysis, therefore, the means were compared using the Scott-Knot test ($p<0.05$) through the software R version 4.1.1 (R Core Team, 2023). In this way, it was possible to visualize which doses have greater statistical relevance to the calculated values.

RESULTS AND DISCUSSION

The data for the concentration of cadmium in the edible part of the plant, previously established in the reference study of cadmium in jambu, by Oliveira (2021), were used to estimate the values obtained in the equations mentioned above. Table 1 shows the mean values calculated for each treatment.

The TRQ values in the leaf, stem and flower of jambu can be observed in fig. 1. The highest values for leaf are in the treatments of 3 $mg.L^{-1}$ and 1$mg.L^{-1}$ and the lowest in the treatments of 6 $mg.L^{-1}$ and 9 $mg.L^{-1}$ respectively. It should be noted that according to the Scott-Knot test, the dose of 3 $mg.L^{-1}$ was the one that most accumulated cadmium in their tissues and the one that came closest to the maximum allowed value ($TRQ<1$). It should be noted that although the dose of 3 $mg.L^{-1}$ came close, it was below the limit dose.

Table 1 - Means of the calculated values of Estimated Daily Intake, Target Risk Quotient and Carcinogenic Risk in relation to cadmium levels in jambu plant parts

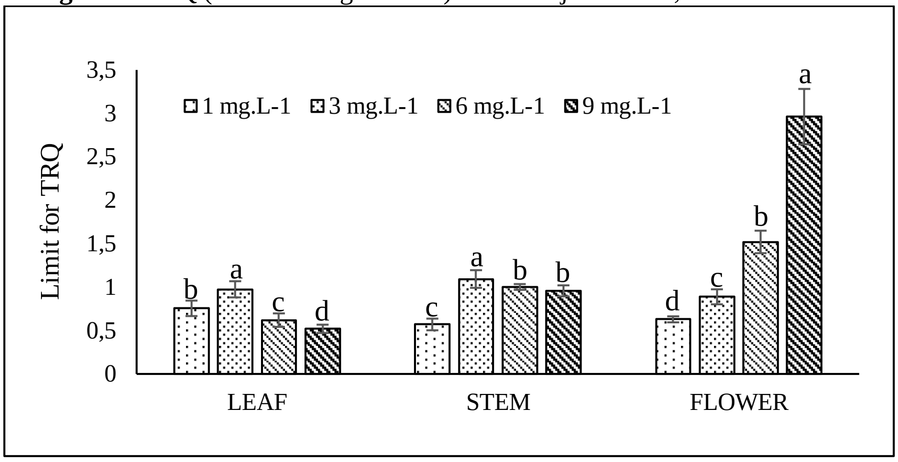
Doses	Leaf			Stem			Flower		
(mg.L^{-1})	EDC	TRQ	CR	EDC	TRQ	CR	EDC	TRQ	CR
1	0,00075	0,7553b	0,00028b	0,00056	0,5698c	0,00021c	0,00062	0,628d	0,00023d
3	0,00097	0,9743a	0,00037a	0,00109	1,0928a	0,00041a	0,00088	0,887c	0,00033c
6	0,00061	0,6196c	0,00023c	0,00100	1,0012b	0,00038b	0,00152	1,520b	0,00057b
9	0,00051	0,5193d	0,00019d	0,00095	0,9565b	0,00036b	0,00296	2,962a	0,00112a
CV	-	*8.51*		-	*8.83*		-	*9.49*	

EDC: Estimated Daily Intake; TRQ: Target Risk Quotient; CR: Carcinogenic Risk. Data were subjected to two-way analysis of variance. Differences among means were determinate using Scott-Knott (p<0.05) test. Source: Authors (2023)

Several authors have already explained in their works the effects that cadmium can generate in humans (OLIVEIRA et al. 2022b; WANG et al. 2021; CWIELĄG-DRABEK et al. 2020; LUCKETT et al. 2012). These damages can be carcinogenic and non-carcinogenic.

The values showed increasing behavior from doses of 1 mg.L^{-1} to 3 mg.L^{-1}, peaking at the dose of 3 mg.L^{-1} before starting to decrease between doses of 6 mg.L^{-1} and 9 mg.L^{-1}. Statistically, the dose that showed less significance was 9 mg.L^{-1}.

Figure 1: TRQ (non-carcinogenic risk) values in jambu leaf, stem and flower.



Bars indicate the standard deviation. Data were subjected to two-way analysis of variance. Differences among means were determinate using Scott-Knott (p<0.05) test. Source: Authors (2023)

The lowest value calculated for TRQ in the stem of jambu was for the dose of 1 mg.L^{-1}, which remained below the limit dose, while the values of 6 mg.L^{-1} and 9 mg.L^{-1} showed no statistical difference between them (Scott-Knot), and the value with the highest result, and above the maximum value established, was the dose of 3 mg.L^{-1}, with a significant difference from the other doses.

Ismael et al (2019) points out that the accumulation in the aerial part of the plant precedes the transport of the element by the roots and stem, where there is a distribution of cadmium throughout the growth of the plant. This fact may explain the presence of cadmium at a level above the established level in the stem of jambu.

The values obtained for the inflorescence in jambu differed in behavior from the other values, being the most significant dose, therefore, the one that offers more non-carcinogenic risk, the 9 mg.L^{-1}. The doses of 1 mg.L^{-1} and 3 mg.L^{-1} were within the maximum limit established (TRQ<1) and the dose of 6 mg.L^{-1} and 9 mg.L^{-1} being above the recommended. Exceeding by 52% and 196% the limit dose, respectively. This behavior shows a high accumulation of cadmium in the flower of jambu as the higher dose to which it is exposed.

According to Qin et al (2019), cadmium accumulated more in the flower of the plant due to a process of the oxidative system, where in the central parts of the plant (stem and leaf) there is a reduction in cadmium uptake and it is translocated to the upper part of the plant (flower). Thus, due to the tolerance system of the plant, there is a brief detoxification before the recovery of growth, a fact that explains the apparent good health of the plant.

Wang and Du (2013) draw attention to the fact of prolonged exposure to cadmium for neurotoxic effects. As well as Chen et al (2018b) calls attention to the fact of high exposure to cadmium through food, given that rice contributed 81% to the consumption of cadmium and vegetables with 19%, and may lead to the development of some non-cancer disease. In the meantime, it is possible to conceive a relationship between the risks scored by the authors and the values found for the flower of jambu.

For the CR in jambu leaves, all the values obtained are above the maximum allowed (0.000006), being the dose of 3 mg.L^{-1} the one that stands out among the other doses (Figure 2).

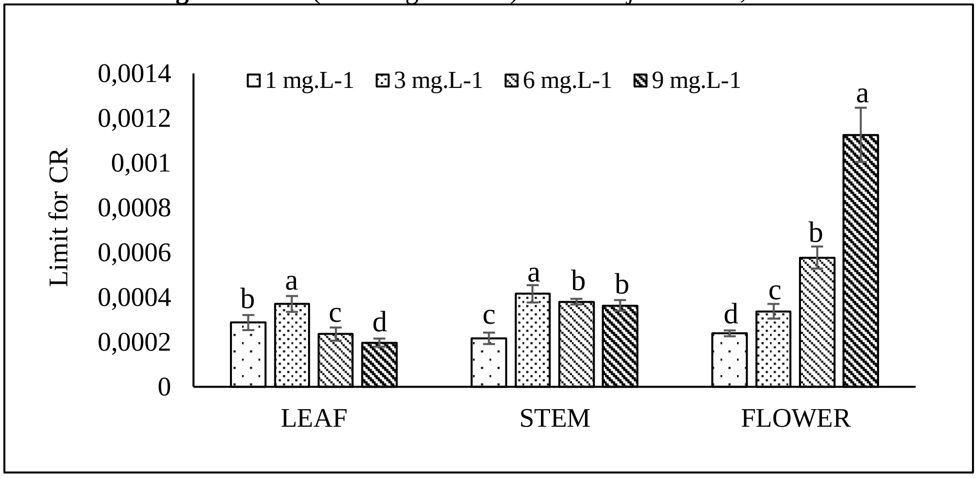
In a study by Zheng et al (2007), which analyzed the transfer factor of the element's mercury, lead, cadmium, zinc and copper in vegetables, cadmium was the element that obtained the highest transfer factor compared to other metals (Zn, Cu, Pb and Hg), and its presence in the leaves was higher than in other parts of the plant, which can be associated with the high accumulation of the element in the jambu leaf, showing high values of carcinogenic risk in the leaf in the present study.

As presented by Cho et al (2013), the periodic consumption of vegetables with cadmium presence can induce the emergence of hormonal cancer in the individual. In this segment, Ke et al (2015) draws attention to the places of cultivation near industrial areas, which can lead to the bioaccumulation of trace elements by plants. This risk can be carcinogenic and non-carcinogenic from the consumption of plants contaminated with cadmium.

Accordingly, Lin et al (2016) and Julin et al (2012) show in their studies the relationship of high cadmium levels in urine as a bioindicator of prolonged heavy metal exposure as well as the possibility of breast cancer development due to this prolonged exposure.

Furthermore, Du et al (2020) indicates that consumption of rice and vegetables grown in areas close to industries that have high levels of cadmium in their tissues is the main route of contamination for the population, and the chance of some individual developing some non-carcinogenic disease, similar to that observed for TRQ in the jambu stem. For the values of carcinogenic risk, all the calculated values were higher than the allowed, being the doses of 6 $mg.L^{-1}$ and 9 $mg.L^{-1}$ not statistically different from each other according to the Scott-Knot test in the stem part. The values of 1 $mg.L^{-1}$ and 3 $mg.L^{-1}$ showed a very significant difference, with the highlight being the dose of 3 $mg.L^{-1}$, the one that was most above the limit dose.

Figure 2 - CR (Carcinogenic risk) values in jambu leaf, stem and flower



Bars indicate the standard deviation. Data were subjected to two-way analysis of variance. Differences among means were determinate using Scott-Knott ($p<0.05$) test. Source: Authors (2023)

Similar to the jambu leaf, in the stem the dose that most demonstrates risk of consumption is 3$mg.L^{-1}$, so it is possible to observe how the values for carcinogenic risk exponentially exceed the limit dose.

Song et al (2015) found a significant association between prolonged cadmium exposure and the development of renal cancer. As well as pointed out by the present study, the chance of any individual developing any carcinogenic disease arising from prolonged exposure to cadmium is very high, in accordance with the presented possibilities of CR in jambu stem.

With similar behavior to the TRQ in flower, the CR presented the dose of 9 $mg.L^{-1}$ as the one that most accumulated cadmium in their tissues and the one that presented the most statistically significant value, as well as being the value with the highest carcinogenic risk. All the other values (6 $mg.L^{-1}$, 3 $mg.L^{-1}$ and 1 $mg.L^{-1}$) had values higher than the recommendable, therefore, all of them present risk to humans of developing a carcinogenic disease.

Yang et al (2016) shows that cadmium tends to accumulate first in the edible parts of the plant (flower) and have a higher accumulation capacity in the aerial part than in the basilar parts of the plant, similarly to the present study, given the high values present in the flower of jambu. In the same segment of this study, Wang et al (2014) points out that individuals who consume cadmium-contaminated vegetables have a high chance of developing some carcinogenic disease.

Accordingly, in the analysis by Huang et al (2021), it points out the values for non-carcinogenicity higher than the established (1), similarly as those presented for the TRQ of jambu stem and flower. According to Hungria et al (2019) the values of jambu can be attributed due to its high bioaccumulative potentiality of the heavy metal.

Thus, as pointed out by Qing et al (2020), a study of cadmium consumption from 1988 to 2018 shows how cadmium exposure increased over time and how it posed a carcinogenic risk to the population. Thus, prolonged exposure to cadmium within the limits scored in this study would be of serious consequences to human health.

Oliveira, et al (2022b) emphasizes that low doses of cadmium positively influence the growth of jambu, a fact that explains the dose of 3 $mg.L^{-1}$ being the dose that was most absorbed by the plant, except the flower, being the most accumulated dose the one of 9 $mg.L^{-1}$. The limit dose for $TRQ<1$, was exceeded in most samples analyzed, and the limit for CR (0.000006) was exceeded in all samples.

In table 2 it is possible to observe the regression models for each variable (TRQ and CR) for the three parts of the plant studied (leaf, stem, flower). As can be seen, all values of carcinogenic risk for the three parts of the plant were above the established maximum value.

In the values of the leaf and stem part of jambu, the same dose showed the highest carcinogenic risk (3 $mg.L^{-1}$), differing in the other doses (1 $mg.L^{-1}$, 6 $mg.L^{-1}$ and 9 $mg.L^{-}$

[1]). It is worth noting that in the stem the doses of 6 mg.L^{-1} and 9 mg.L^{-1} did not differ from the statistical point of view.

Table 2 - Regression model for edible parts of jambu with cadmium.

Parts of the plant	Variables	Regression analysis	Adjusted R^2	*p-value*
Leaf	TRQ	$y = -0.0081D^{2**} + 0.040D + 0.7869$	0,5313	0,04637967
	CR	$y= -3.11D^{2**} +1.521D+0.0002$	0,5313	0,04637967
Stem	TRQ	$y = -0.020D^{2**} +0.2378D+0.4171$	0,6504	2,72913E-05
	CR	$y= -7.679D^{2**} +9.0375D+0.00015$	0,6504	2,72913E-05
Flower	TRQ	$y= 0.0342D^{2**} -0.0567D+0.6818$	0,9628	2,78259E-06
	CR	$y= 1.301D^{2**} -2.157D+0.0002$	0,9628	2,78259E-06

** significant at 5% probability (F test); D=dose; D^2=dose squared. Source: Author (2023)

The dose in the flower part of jambu was different from the others, and the one that showed the highest value was the dose of 9 mg.L^{-1}. The difference between the dose that showed the highest value in the stem and the other parts of the plant (leaf and stem) were significant at 9 mg.L^{-1}; at 3 mg.L^{-1}).

Of all the values calculated for TRQ and CR in the three parts of the plant, the CR is 100%, given that the maximum allowed value for CR (1x10-6) was exceeded in all three parts of the plant studied. Due to the high toxicity of cadmium and the ability of jambu to tolerate and accumulate it in its tissues. The chance of an individual developing some type of carcinogenic disease due to the consumption of contaminated jambu is 100%, based on the fact that even at the lowest calculated dose (1 mg.L^{-1}) the value extrapolated the maximum allowed.

For the variable TRQ, the risk of an individual developing a non-carcinogenic disease was 66.7% if the consumption came from the stem or flower of jambu, since in the leaf the accumulated cadmium content was in accordance with the established maximum (TRQ<1).

Taking into account all the variables studied, the chance of an individual developing some type of disease, whether carcinogenic or non-carcinogenic derived from the consumption of the leaf, stem, or flower of the contaminated vegetable is 83.3%.

Furthermore, Oliveira et al (2022a) points out that the jambu concentrates most of the cadmium in the edible region of the plant, which generates concern about its consumption. Emphasizing that in their research, all values found in the edible part of the plant were above the limits established in Brazil.

In Brazil, according to the Normative Instruction No. 88 of March 26, 2021 of the National Health Surveillance Agency, the maximum tolerated limit of contaminant in food for vegetables is 0.05 $mg.kg^{-1}$ after washing. However, because jambu is a plant also derived from family farming, sometimes this limit may not be observed.

Therefore, taking into account that jambu is a cadmium-tolerant plant, and even in soils with high doses of the heavy metal it can grow, the risk offered to consumers of this plant is very high at the prospect of cultivation in potentially contaminated soil or in the vicinity of sources of contamination.

CONCLUSIONS

Jambu was shown to be a plant that possibly poses a risk to the population if contaminated with cadmium. The values for TRQ and CR were above the maximum allowed value, except for the leaf for TRQ. For the jambu leaf and stem, the most statistically significant dose was 3 $mg.L^{-1}$, which poses the greatest carcinogenic or non-carcinogenic risk. In the jambu flower, the most statistically significant dose was 9 $mg.L^{-1}$, both for CR and TRQ. Given that it is the highest dose of the treatment, the consumption of jambu flower offers much more risk due to having accumulated the highest dose under study.

In summary, for carcinogenic risk all values (1, 3, 6 and 9 $mg.L^{-1}$) were above the dose limit of 0.000006. For non-carcinogenic risk, for leaves all values were below the threshold dose. For stem, only one value was above the limit dose (3 $mg.L^{-1}$) and the value of 6 $mg.L^{-1}$ was equal to the limit dose. For flower, the doses that were above the limit dose were 6 $mg.L^{-1}$ and 9 $mg.L^{-1}$ respectively.

Thus, it is clear that the jambu contaminated with cadmium generates health impacts on humans, both carcinogenic and non-carcinogenic, but this fact is more profound due to the social and economic context of the country. Therefore, the present research draws attention to the cultivation areas in the vicinity of industrial activities and to the danger of trace element bioaccumulating plants, which can carry various elements (not only cadmium) into the human food chain. It is suggested that the theme be further explored with other plants used in the local cuisine and how they behave in the presence of trace elements.

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