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Evaluation of the hepatoprotective effect of *Zea mays* beards in *Rattus norvegicus*

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Abstract

The aim of this study is to contribute to the management of drug-induced hepatitis through the valorization of *Zea mays* beards. The aqueous extract of *Zea* mays beards was obtained by decoction. Secondary metabolites were searched for by the colorimetric method and minerals were searched for by the calcination – mineralization method. The study of the acute toxicity of the aqueous extract of *Zea mays* beards was conducted orally, following the OECD Guideline 423. Hepatotoxicity was induced by gavage with paracetamol 1000 mg on 7 days. The results of the study indicate that the aqueous extract of *Zea mays* beards contains secondary metabolites, including alkaloids, saponins, polyphenols, flavonoids, tannins, quinones and minerals including chromium, potassium, iron, zinc, magnesium and copper. The aqueous extract of *Zea mays* beards is not toxic orally up to a dose of 5000 mg/kg body weight and corrected abnormally high levels of alanine aminotransferase and aspartate aminotransferase. This normalization of alanine aminotransferase and aspartate aminotransferase levels would be linked to the flavonoids and zinc present in said extract. This study reveals the hepatoprotective effect of the aqueous extract of *Zea m*ays beards.

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Introduction

Some conventional medicines and herbal recipes can affect the functioning of the liver or damage it. Drug-induced hepatitis is on the rise and is believed to be the cause of many deaths and the withdrawal of many drugs from the pharmaceutical industry's market. The advent of HIV infection has contributed to the production of hepatotoxic antiretroviral substances. Also, anti-tuberculosis drugs are thought to be hepatotoxic (Durand, 1998). In addition, all therapeutic classes are concerned (Larrey, 2002) because drugs can be responsible for liver pathology by negatively impacting liver cells such as hepatocytes, cholangiocytes, endothelial cells and Ito cells (Larrey, 2003). The liver is the first target because it metabolizes everything that enters through the mouth (Danielle and Sidney, 2023).

The liver is involved in all biochemical pathways of growth, the immune system, metabolism and reproduction (Ward and Daly, 1999). Thus, any attack on this organ constitutes a threat to survival. The bile that is secreted by the liver plays a role in digestion and has other functions through which the body maintains its balance. It is an excretory function that allows the excretion of different waste products produced by the human body. In addition, bile has a role in controlling cholesterol because it helps eliminate excess cholesterol. Finally, bile has a detoxifying function because the bile salts it contains are able to degrade certain poisons such as medicines, alcohol and certain drugs (Coulibaly, 2024). *Zea mays* beards are liver detoxifiers because they are bile stimulants and thinners and therefore depuratives (Bernard, 2018). This is what justified the choice of the theme : "Evaluation of the hepatoprotective effect of *Zea mays* L. beards in *Rattus norvegicus* of the wistar strain". The general objective is to contribute to the management of drug-induced hepatitis.

Materials and methods

Materials

The vegetable material was composed of beards of *Zea mays* and the animal material was composed of albino rats of the wistar strain.

Methods

Obtaining Zea mays beards

To obtain the plant material, a maize field was created in May 2023 just after the botanical garden of the Peleforo GON COULIBALY University, after the agreement of the heritage manager of the said university. With the intention of obtaining organic corn beards, the field was created with corn of the LG 501 variety and maintained without the use of pesticides or chemical fertilizers. Two months after sowing, the stigmata or corn barbs appeared on the ears of maize. After two weeks of appearance, the corn husks were harvested and dried away from light for six weeks.

Preparation of aqueous extract of *Zea mays* beards

The beards of Zea mays dried in the dark for six weeks were taken to the laboratory to be made into powder using the electric grinder (IKAMAG). One hundred (100) grams of corn beard powder was added to a pot containing a quart of boiling distilled water and this set was brought to a boil for 15 to 20 minutes. After cooling, a first filtration was carried out on a sieve. Then, two filtrations on hydrophilic cotton were carried out and the collected filtrate was put in a crystallizer and heated at 40 °C for complete drying. After drying, the dry mass at the bottom of the crystallizer was scraped off and made into a fine powder and the latter constituted the aqueous extract of the beards of *Zea mays* (Guédé-guina *et al.*, 1993).

Phytochemical screening and micronutrient assay in Zea mays beards

The search for secondary metabolites in the aqueous extract of the beards of *Zea mays* was carried out by the colorimetric method (Trease and Evans, 2002). The determination of trace elements was done by calcination – mineralization (Clement and Francoise, 2003).

Study of the acute toxicity of the aqueous extract of Zea mays beards

The acute toxicity study of the aqueous extract of *Zea mays* beards was conducted by the oral route and was conducted in accordance with OECD test guideline

(OCDE 423, 2001). The test design used in the study was the one using an initial dose of 2000 mg/kg body weight (bw) because *Zea mays* beards are more or less known for their non-toxicity. Three 20-week-old female albino rats of wistar strain with a homogeneous mean weight of 144.33 ± 0.45 g, were fasted for 12 hours prior to administration of the aqueous extract of *Zea mays* beards. The amount of *Zea mays* extract to be force-fed to female rats was 1 mL per 100 g of body weight. After force-feeding each spleen, they were subjected to continuous observation for 14 days with particular attention during the first 24 hours in order to identify apparent clinical signs and possible deaths. After the 14 days of observation of female rats subjected to the 2000 mg/kg bw dose, the immediate upper dose of 5000 mg/kg bw was then administered to three additional albino female rats of the wistar strain after 12 hours of fasting. The latter had a homogeneous mean weight of 146 ± 0.32 g, aged 20 weeks. The amount of *Zea mays* extract to be force-fed to female rats was based on the OECD test guideline 423 of 1 mL per 100 g body weight. After force-feeding each spleen, they were also subjected to continuous observation for 14 days with special attention during the first 24 hours in order to identify apparent clinical signs and possible deaths.

Induction of hepatotoxicity

The hepatoprotective activity of the aqueous extract of *Zea mays* beards was tested according to the curative model (Kamisan *et al.*, 2013). Thirty (30) male and female rats, albino of wistar strain, with an average weight of 197.17 ± 0.55 g, aged 24 weeks (6 months) were used. The rats were divided into five homogeneous batches of six (06) rats each, fasted for 12 hours and force-fed according to the distribution below :

On the 8th day, the rats in the different batches were anesthetized by inhalation of ether and the blood of each rat was drawn from its tail in red tubes for transaminase (Alanine aminotransferase, Aspartate aminotranferase) determination. On the 15th day, the rats in the different batches were again anesthetized by inhalation of ether and the blood of each rat was taken from its tail in red tubes for the determination of transaminases : Alanine aminotransferase, Aspartate aminotranferase.

Alanine aminotansferase essay

The amine group is transferred enzymatically by the Alanine Aminotransferase present in the sample from Alanine to the carbon atom of 2-oxoglutarate producing pyruvate and L-glutamate. Pyruvate is reduced to lactate by the LDH present in the reactant with simultaneous oxidation of NADH to NAD. The reaction is followed by measuring at 340 nm, the decrease in absorbance due to the oxidation of NADH to NAD+. This decrease is proportional to the activity of Alanine Aminotransferase present in serum by the kinetic method (Gella *et al.*, 1985).

Aspartate aminotransferase assay

The amine group is transferred enzymatically by the Aspartate Aminotransferase present in the sample from the Aspartate to the carbon atom of the 2-oxoglutarate producing oxaloacetate and L-glutamate. The reaction is followed by measuring at 340 nm, the decrease in absorbance due to the oxidation of NADH to NAD+. This decrease is proportional to the activity of aspartate aminotransferase present in serum by the kinetic method of Gella *et al.* (1985).

Results

Secondary metabolites and trace elements

Phytochemical analyzes revealed the presence of alkaloids, saponins, polyphenols, flavonoids, gallic tannins, catechin tannins and quinones in the aqueous extract of *Zea mays* awns. However, sterols and terpenes were absent in said extract (Table 2). The determination of trace elements revealed the presence of minerals such as chromium, potassium, iron, zinc, magnesium and copper. Their contents are mentioned in Table 3.

Acute toxicity

Oral administration of the aqueous extract of *Zea mays* beards to female rats, at doses of 2000 and 5000 mg/kg body weight (bw), did not cause any mortality during the 14 days of observation. No

significant change was also observed in the behavior of the latter. During the acute oral toxicity test of the aqueous extract of *Zea mays* beards, there was weight gain in female rats because their average weight (197.12 ± 0.55 g) on day D_0 respectively increased to 203.65 ± 0.28 and 210.9 ± 0.09 g on days D_7 and D_{14}.

Table 1. Phytochemical screening of the aqueous extract of *Zea mays* beards.

• Batch 1 :	having received distilled water for 14 days,
• Batch 2 :	poisoned with paracetamol 1000 mg at a dose of 2500 mg/kg bw for 7 days and having received distilled water from the 8th to the 14th day,
• Batch 3 :	intoxicated with paracetamol 1000 mg at a dose of 2500 mg/kg bw for 7 days and treated with aqueous extract of *Zea mays* at a dose of 100 mg/kg bw from the 8th to the 14th day,
• Batch 4 :	poisoned with paracetamol 1000 mg at a dose of 2500 mg/kg bw for 7 days and treated with the aqueous extract of *Zea mays* at a dose of 200 mg/kg bw from the 8th to the 14th day,
• Batch 5 :	intoxicated with paracetamol 1000 mg at a dose of 2500 mg/kg bw for 7 days and treated with milk thistle (hepatoprotective drug) at a dose of 150 mg/kg bw from the 8th to the 14th day.

Transaminase concentrations

Figure 1 represents the aspartate aminotransferase concentrations of rats from batches 1 ; 2 ; 3 ; 4 and 5 on the 7th and 14th days of the hepatotoxicity test. The determination of aspartate aminotransferase in rats from the control group not poisoned with paracetamol (batch 1) on the 7th day of the test gave a concentration of 6.50 ± 0.21 IU/L while the aspartate aminotransferase concentrations in the rats batches 2 ; 3 ; 4 and 5 poisoned with paracetamol at a dose of 2500 mg/kg body weight were respectively 11.27 ± 0.12 ; 10.77 ± 0.23 ; 20.37 ± 0.49 and 28.6 ± 0.83 IU/L. The aspartate aminotransferase concentrations of rats from batches 2 and 3 showed a highly significant increase ($p < 0.01$) compared to that of rats from the control batch (batch 1). As for the aspartate aminotransferase concentration of rats from batch 4, it experienced a very significant increase ($p < 0.001$) compared to that of rats from the control batch (batch 1) on the 7th day. Concerning the rats from batch 5, their aspartate aminotransferase concentration experienced a very highly significant increase ($p < 0.0001$) compared to the aspartate aminotransferase concentration of the rats from batch 1. From the 8th to the 14th day, the rats in the control batch (batch 1) and those in batch 2 received distilled water while the rats in batches 3 and 4 were respectively treated with *Zea mays* beards at the respective doses of 100 and 200 mg/kg body weight. As for the rats in batch 5, they were treated with Milk Thistle at a dose of 150 mg/kg body weight from the 8th to the 14th day.

The determination of aspartate aminotransferase in rats from the control group (batch 1) on the 14th day of the hepatotoxicity test gave a concentration of 6.60 ± 0.23 IU/L which was substantially equal ($p > 0.05$) to that (6.50 ± 0.21 IU/L) of the 7th day of the test. Concerning the aspartate aminotransferase concentration (15.40 ± 0.06) of rats poisoned with paracetamol and untreated (batch 2), it experienced a very significant increase ($p < 0.001$) on the 14th day compared to the concentration of rats of the control batch (6.60 ± 0.23 IU/L) from the 14th day.

Concerning rats poisoned with paracetamol and treated with the aqueous extract of *Zea mays* beards at doses of 100 mg/kg body weight (batch 3) ; 200 mg/kg body weight (batch 4), and Milk Thistle at a dose of 150 mg/kg body weight (batch 5), their aspartate aminotransferase concentrations were respectively 8.10 ± 0.01 ; 6.70 ± 0.01 and 7.03 ± 0.01 IU/L on the 14th day of the test. These aspartate aminotransferase concentrations in rats from batches 3 ; 4 and 5 of the 14th day decreased considerably so as to have aspartate aminotransferase concentrations very close ($p > 0.05$) to that of the rats in the control group (6.60 ± 0.23 IU/L) of the 14th day.

Table 2. Phytochemical screening of the aqueous extract of *Zea mays* beards.

Phytochemical compounds	Aqueous extract of *Zea mays* beards
Alkaloids	+
Saponins	+
Polyphenols	+
Flavonoids	+
Catechin and gallic Tannins	+
Sterols and Terpenes	-
Quinones	+

(+) : presence (-) : absence

Each histogram represents the mean ± standard deviation; n = 6 ; ···· P < 0.0001: very highly significant increase in the concentration of aspartate aminotransferase compared to that of control rats not intoxicated by paracetamol (batch 1) ; ··· P < 0.001: very significant increase in the concentration of aspartate aminotransferase compared to that of control rats not intoxicated by paracetamol (B1 = batch 1) ; ·· P < 0.01: highly significant increase in aspartate aminotransferase concentration compared to control rats not intoxicated by paracetamol (batch 1) ; P > 0.05: aspartate aminotransferase concentration not significant (ns) compared to that of control rats not poisoned by paracetamol (batch 1) ; B2 = batch : batch of rats poisoned with paracetamol 1000 mg for 7 days and untreated ; B3 = batch 3: batch of rats poisoned with paracetamol 1000 mg for 7 days and treated for 7 days with the aqueous extract of Zea mays beards 100 mg/kg bw ; B4 = batch 4: batch of rats poisoned with paracetamol 1000 mg for 7 days and treated for 7 days with the aqueous extract of Zea mays beards 200 mg/kg bw ; B5 = batch 5: batch of rats poisoned with paracetamol 1000 mg for 7 days and treated for 7 days with milk thistle 150 mg/kg bw.

Figure 2 represents the alanine aminotransferase concentrations of rats from batches 1 ; 2 ; 3 ; 4 and 5 on the 7th and 14th days of the hepatotoxicity test. The alanine aminotransferase concentration in the rats from the control group not poisoned with paracetamol (batch 1) on the 7th day of the hepatotoxicity test was 47.87 ± 0.73 IU/L while the alanine aminotransferase concentrations in the rats of batches 2 ; 3 ; 4 and 5 poisoned with paracetamol at a dose of 2500 mg/kg body weight were respectively 67.60 ± 2.26 ; 65.00 ± 2.89 ; 65.07 ± 1.55 and 92.60 ± 1.70 IU/L on the 7th day. These concentrations of alanine aminotransferase from batches 2 ; 3 ; 4 and 5 experienced a highly significant increase ($p < 0.01$) on the 7th day of the hepatotoxicity test compared to that of the rats in the control group (47.87 ± 0.21 IU/L). For the rats from batch 5, their alanine aminotransferase concentration experienced a very highly significant increase ($p < 0.0001$) compared to that of the rats from the control group (batch 1).

Table 3. Trace elements content of the aqueous extract of *Zea mays* beards.

Trace elements	Contents (µg/g of dry extract) aqueous extract of *Zea mays* beards
Chromium	0,39 ± 0,10
Potassium	1651 ± 0,84
Iron	1,83 ± 0,32
Zinc	61,17 ± 0,43
Magnesium	577,09 ± 0,75
Copper	157,58 ± 0,68

From the 8th to the 14th day of the hepatotoxicity test, the rats in the control group (batch 1) and those in batch 2 received distilled water while the rats in batches 3 and 4 were respectively treated with the extract aqueous of *Zea mays* beards at respective doses of 100 and 200 mg/kg body weight. As for the rats in batch 5, they were treated with Milk Thistle at a dose of 150 mg/kg body weight from the 8th to the 14th day of the test. The determination of alanine aminotransferase in rats from the control group (batch 1) on the 14th day of the experiment gave a concentration of 47.97 ± 0.61 IU/L which was significantly similar ($p > 0.05$) to that of rats from the control group (47.87 ± 0.73 IU/L) on the 7th day of the hepatotoxicity test. Regarding rats poisoned with paracetamol and not treated (batch 2), the alanine aminotransferase concentration (80.63 ±

2.13) of these rats experienced a very highly significant increase ($p < 0.0001$) on the 14th day compared to the alanine aminotransferase concentration of rats from the control group (47.97 ± 0.61 IU/L) on the 14th day. With regard to rats poisoned with paracetamol and treated with the aqueous extract of *Zea mays* beards at doses of 100 mg/kg body weight (batch 3) and 200 mg/kg body weight (batch 4), and milk thistle at the dose of 150 mg/kg body weight (batch 5), their alanine aminotransferase concentrations were respectively 49.97 ± 0.01 ; 48.01 ± 0.01 and 49.06 ± 0.01 IU/L on the 14th day of the test. These alanine aminotransferase concentrations in rats from batches 3 ; 4 and 5 of the 14th day decreased considerably so as to have alanine aminotransferase concentrations very close ($p > 0.05$) to that of the rats in the control group (47.97 ± 0.61 IU/L) of the 14th day. The aqueous extract of *Zea mays* beards at doses of 100 and 200 mg/kg body weight as well as milk thistle at a dose of 150 mg/kg body weight had the same ($p > 0.05$) hepatoprotective effect at 14th day.

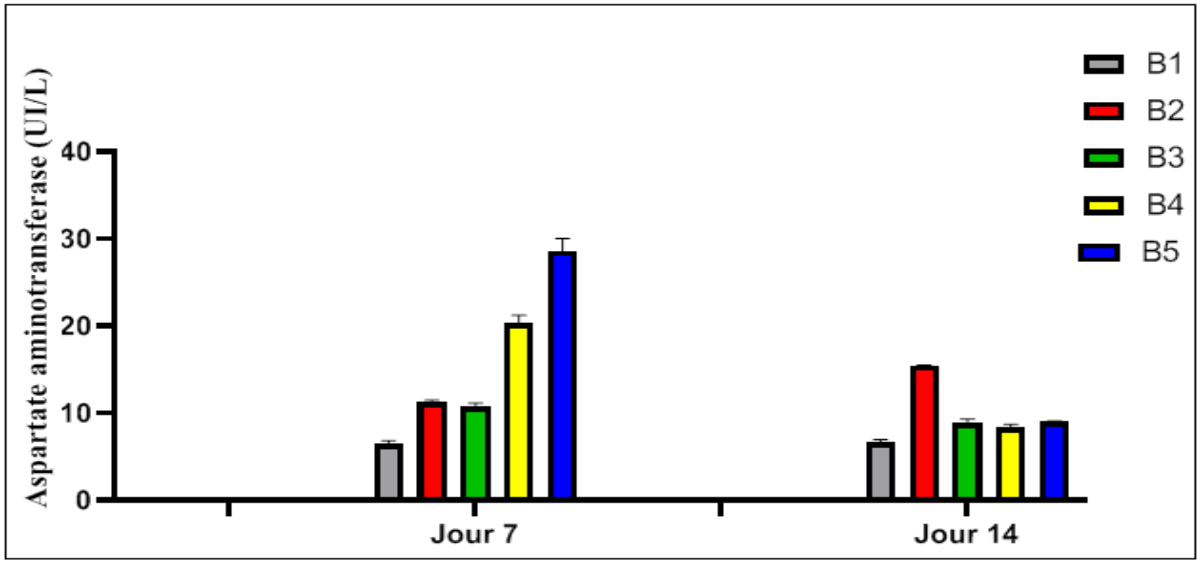

Fig. 1. Aspartate Aminotransferase concentration of rats on days 7 and 14.

Each histogram represents the mean ± standard deviation ; n = 6 ; …. $P < 0.0001$: very highly significant increase in alanine aminotransferase concentration compared to control rats not intoxicated by paracetamol (batch 1) ; .. $P < 0.01$: highly significant increase in alanine aminotransferase concentration compared to control rats not intoxicated by paracetamol (B1= batch 1). $P > 0.05$: non-significant alanine aminotransferase concentration (ns) compared to that of control rats not intoxicated by paracetamol (batch 1); B2 = batch 2: batch of rats poisoned with paracetamol 1000 mg for 7 days and untreated; B3 = batch 3: batch of rats poisoned with paracetamol 1000 mg for 7 days and treated for 7 days with the aqueous extract of Zea mays beards 100 mg/kg bw; B4 = batch 4: batch of rats poisoned with paracetamol 1000 mg for 7 days and treated for 7 days with the aqueous extract of Zea mays beards 200 mg/kg bw; B5 = batch 5: batch of rats poisoned with paracetamol 1000 mg for 7 days and treated for 7 days with milk thistle 150 mg/kg bw. $P > 0.05$: non-significant alanine aminotransferase concentration (ns) compared to that of control rats not intoxicated by paracetamol (batch 1).

Discussion

Phytochemical analyses revealed the presence of polyphenols, flavonoids, catechetical tannins, saponosides and quinones in the aqueous extract of *Zea mays* beards by decoction. These results are corroborated by those of Hassani (2023) who found these same secondary metabolites in the aqueous extract of *Zea mays* beards by infusion.

The determination of trace elements in the aqueous extract of *Zea mays* beards revealed the presence of

chromium, iron, zinc, magnesium, copper and potassium. Except for chromium, the trace elements found in the aqueous extract of *Zea mays* beards are the same trace elements found by Zohoungbogbo *et al.* (2018) in *Zea mays* seeds. The absence of death and significant change in the behaviour of rats at the extreme dose of 5000 mg/kg body weight shows that the aqueous extract of *Zea mays* beards is not toxic.

These results are consistent with those of Singh *et al.* (2009) who showed that methanolic extract of *Zea mays* silk was not toxic up to 2000 mg/kg bw.

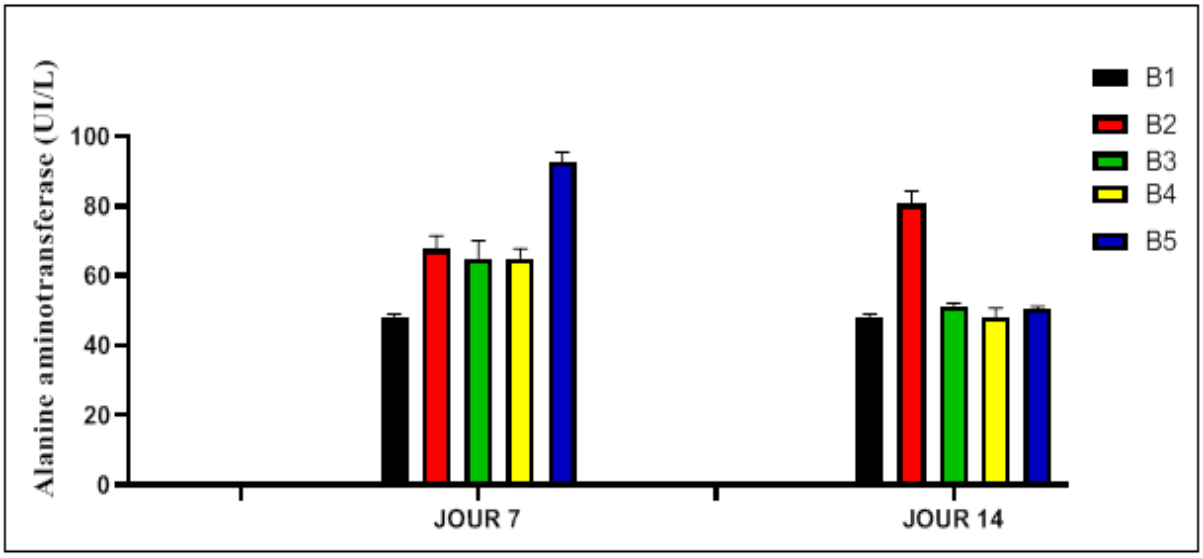

Fig. 1. Alanine aminotransferase concentration of rats on days 7 and 14.

Hepatotoxicity was induced in this study by EFFERALGAN 1000 mg in the form of film-coated tablets containing paracetamol. EFFERALGAN, which contains paracetamol, is an analgesic and an antipyretic. For any drug, after its absorption, it is metabolized and eliminated by the liver. If overdosed, the drug becomes toxic.

This is the case with paracetamol, which, taken in high doses, can cause liver disorders (Gujrati *et al.*, 2007). Quantification of serum transaminase concentrations (alanine aminotransferase and aspartate aminotransferase) is a method for assessing hepatotoxicity (Himmerich *et al.*, 2005). Elevated serum alanine aminotransferase and aspartate aminotransferase concentrations in intoxicated rats indicated cell lysis because these enzymes are intracellular (Adesanoye and Farombi, 2010). Also, the disturbances in liver function caused by paracetamol were explained by the elevated concentrations of alanine aminotransferase and aspartate aminotransferase. In addition, elevated alanine aminotransferase concentrations were a more specific indicator of liver injury than that of aspartate aminotransferase because elevated concentrations of aspartate aminotransferase can also be linked to muscle, cardiac or kidney damage (Dufour *et al.*, 2000 ; Ozer *et al.*, 2008 ; Ujah *et al.*, 2013).

The normalization of alanine aminotransferase and aspartate aminotransferase concentrations in rats treated with the aqueous extract of *Zea mays* beards and milk thistle (containing sylimarin : the hepatoprotective reference molecule) could be explained by reconstruction of liver lesions. This reconstruction of liver lesions is thought to be linked to the flavonoids present in the aqueous extract of Zea mays beards because the flavonoids present in the sylimarin extracted from *Silybum marianum* are protective and reconstructive of liver lesions (Luper, 1998 ; Kazemifar *et al.*, 2012). This reconstructive activity of hepatocytes is also linked to the zinc present in the aqueous extract of *Zea mays* beards. Zinc is a trace element that has hepatoprotective effects against various hepatotoxic agents and antioxidant functions (Marchesini *et al.*, 1996).

Conclusion

It appears from this study that the aqueous extract of *Zea mays* beards has a hepatoprotective activity.

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Conflict of interest

No conflicts of interest were identified by the authors

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