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Full Length Research Paper

Biochemical effectiveness in liver detoxication of fresh pineapple (*Ananas comosus*) with the wistar rats, previously intoxicated by Doliprane®

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The effect of hepatic detoxication with the help of fresh pineapple (*Ananas comosus*), was evaluated on 28 wistar albinos rats previously intoxicated by DOLIPRANE® containing 20% of paracetamol. Four batches consisting, each them of 7 animals were formed. Batch n° 1, was neither intoxicated nor treated. Batch n° 2 was intoxicated for 2 weeks at the rate of two two (2) grams of DOLIPRANE® per kilogramme of live weight per day, then treated for 4 weeks with 13 mg of fresh pineapple per kg of live weight per day. Batch n°3 was intoxicated in the same way as batch n°2, but received 26 mg of fresh pineapple during 4 weeks. Batch n°4, was intoxicated for two weeks with the same daily amount of DOLIPRANE® and did not receive any treatment with pineapple. The rates of Alkaline Phosphatase (ALP), Glutamate Oxaloacetic Transaminase (GOT) and Glutamate Pyruvate Transaminase (GPT) enzymes were ganged. As for batch n°4, the values of those enzymes underwent a highly significant increase on the threshold of 0.1% when compared with the other three batches. ALP concentrations decreased from 406.67 ± 7.17 to 223.67 ± 3.28 for batch n°2 after the treatment with the pineapple. Concerning the GPT, value significantly decreased, passing from 242.67 ± 31.67 to 106 ± 2.31 for batch n° 2. As for the GOT, its rate passed from 184.67 ± 3.75 to 117.33 ± 2.73 for batch n°2, without any significance level on the threshold of 5%, comparing batches n° 2 and n°3. It emerges from this study that overdosing of DOLIPRANE® (2 g/kg of live weight) affected the biochemical level, the normal functioning of the liver of the wistar rats intoxicated *per os*. Fresh pineapple had a reconstructive effect on the hepatic metabolism of the intoxicated rats.

Key words: Liver detoxication, pineapple, doliprane®, enzymes, wistar rats.

INTRODUCTION

The cytolyse hepatic syndrome is definite like the elevation of seric activity of the enzymes: Alkaline Phosphatase and transaminases (Capron, 1989). The liver plays an important part of synthesis, detoxication and homeostasia as well in animals as in human being. The deterioration of hepatocytes provokes an hepatocellular insufficiency which leads to liver malfunction (Shang, 1999). In human medicine, the frequency in liver deterioration has been significantly alarming these years. For instance, it has been noticed an increase in the number of liver cancers coming along on top of cirrhosis due to hepatitis C virus. Today, 50% of carcinomas hepatocellulars develop along with hepatitic C virus, both in U.S.A and Europe; this rate may reach 80% in Japan (Shiina 2005). In Western countries, 30% of the people suffering from B or C viral cirrhoses are likely to suffer from a carcinome hepatocellular within ten years (Anne, 2005). In Africa and in Asia, aflatoxin B1 produced by *Aspergillus flavus* is a carcinogen and it participates in a carcinogenic synergy in patients already suffering from B hepatitis.

Still in Africa, the uncontrolled use of certain pharmaceutical products brings about liver alterations which result in an ongoing appearance of hepatocellular carcinoma.

Thus, paracetamol for instance, a widely used molecule, ingested by an adult on the basis of a single dosage vary from 10 to 15 grams/day for several weeks; can provoke a serious hepatose (Shiina, 2005). At the same moment, classical chemotherapies become more and more ineffective for the treatment of complicated liver deteriorations (Anne, 2005). In the face of such a situa

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tion, medicinal plants stand for an appreciable therapeutic alternative in lots of African countries where the richness of vegetable biodiversity goes without saying. Recourse to those plants is also justified by the fact that imported drugs are not always accessible to certain strata of the society, because of their prohibitive costs (Sofowora, 1996).

This study aims at evaluating the particular virtue of pineapple, in relation to liver detoxication as far as Wistar rats previously intoxicated with DOLIPRANE ® are concerned.

MATERIAL AND METHODS

Material

The healthy animal supply consisted of 28 albinos male rats belonging to the wistar stock five months old weighing each, on average 150 g. They were distributed in four batches of 7 animals bred in individual cage. The DOLIPRANE®, which was used for the induction of intoxication to the liver contained 20% of paracetamol.

The vegetable supply consisted of the peduncle of fresh *Ananas comosus*. This fresh peduncle was weighed and distributed to the rats according to their weight. In addition, they received a food standard *ad libitum*. The pineapple contained 13.51% of a determined dried matter resulting from a 24 h stay of the peduncle in a drying oven, the temperature of which was 100°C.

METHODS

The experimentation is realised in the Research Laboratory of Appliqued Biology located in Abomey-Calavi's University, Atlantic Department, Republic of Benin from January to March, 2007.

Batches constitution

Batch n°1, the negative control batch, received neither DOLIPRANE® nor fresh pineapple.

Batch n°2 received DOLIPRANE® at the rate of 2 g/kg of live weight (LW) per day for 2 weeks and was then treated with the help of fresh pineapple at the rate of 13 mg /kg of LW per day for 4 weeks.

Batch n°3 received DOLIPRANE® at the rate of 2 g/kg of LW per day for 2 weeks and was then treated with fresh pineapple at the rate of 26 mg/kg of LW for 4 weeks.

Batch n°4, the positive control batch, received DOLIPRANE® at the rate of 2 g/kg of LW per day for 2 weeks and didn't undergo any treatment with fresh pineapple till the end of the trial.

Blood taking and dosage of alkaline phosphatase and transaminases

2 ml of blood was taken from the caudal vein into a dry serum tube (Gosselin 59522 Hazebrouck France)

The blood was taken on the basis of day 0 (J0); day 14 (J14) and day 42 (J42) from batches n°1, 2, 3 and 4. The serum got, following a 5 m centrifugation was used for the enzyme dosage. The data were analysed using techniques described by Reed and Herrara which are summarized in recent editions of Tietz's textbook.

Preparing of the DOLIPRANE® for the rats' intoxication

Following the search for DL50 (4 g/kg of LW), it was agreed on 2 g of DOLIPRANE® per kg of LW as the amount likely to induce the intoxication of the wistar rats. This amount was dissolved in 2 ml of water and given individually *per os* to the rats.

ANOVA test was used to calculate the average serum rates of the various enzymes. STUDENT- NEWMAN and KEULS test allowed these averages in the case of significant differences.

RESULTS

Alkaline Phosphatase (ALP) serum levels

Following the treatment of the intoxicated rats with the help of fresh pineapple, ALP concentrations decreased from 406.67 ± 7.17 to 223.67±3.28 for batch n°2 and from 408.33 ± 2.03 to 222.67 ± 3.71 for batch n°3. At the beginning of the experimentation, there is no significant difference among the four batches on the threshold among of 5%. On J14, those values underwent a neat increase among all the intoxicated batches. At the end of the treatment with the help of fresh pineapple, that enzyme concentration almost decreased by half in batches n°2 and n°3. On the other hand, the alkaline Phosphatase levels increased more and more in batch n°4 with a most highly significant difference on the threshold of probability of 0.1% between the alkaline Phosphatase plasma levels in batches n°2 and n°3 from J14 to J42 (Table 1).

The levels of serum glutamate pyruvate transaminase (GPT)

Concerning the GPT, value significantly decreased, passing from 242.67 ± 31.67 to 106 ± 2.31 for batch n° 2 and from 248.67 ± 35.89 to 118.33 ± 11.67 for batch n°3.

At the beginning of the trial, there was no significant difference among the various batches on the threshold of 5%. Following the induction of the toxicity to the liver with DOLIPRANE®, there appears a significant difference on J14 between batch n°1 and the three other batches on the threshold of 0.1%. At the end of the experimentation, the values 61.6 ± 10.41 and 295 ± 2.64 were respectively got on the level of batch n°1 and batch n°4.

The difference is highly significant between those batches on the threshold of 0.1%. It is all one at the end of the experimentation between the values in batches n°2 and n°3 compared with batch n°4. At the end of the experimentation, the values in batches n°2 and n°3 significantly decreased in comparison with J14, but they didn't reach the level of batch n°1 (Table 2).

The levels of serum glutamate oxaloacetic transaminase (GOT)

The rate of the GOT passed from 184.67 ± 3.75 to 117.33 ± 2.73 for batch n°2 and from 181 ± 5.51 to 114.64 ± 4.83 for batch n°3, without any significance level on the threshold of 5%. At the beginning of the trial, there was no significant difference between all the batches on

Table 1. Level of alkaline phosphatase (ALP).

Batches	Alkaline Phosphatase in UI/L		
	J0	**J14**	J42
Batch n°1	134,33±2,96 a	138±2,37 a	140,67±3,10 a
Batch n°2	137,33±3,93 a	406,67±7,17 b	223,67±3,28 b
Batch n°3	139,33±2,18 a	408,33±2,03 b	222,67±3,71 b
Batch n°4	140±2,52 a	437,30±1,85 c	450±1,92 c
Probability	0,75 ns	0,0009***	<0,0001***

*** Very highly significant difference on the threshold of 0.1%
Ns non significant difference on the threshold of 5%. Average values followed by the same letter are non-significantly different on the threshold of 5% probability. Those followed different letters are significantly different**.**
Batch n°1: control batch, neither DOLIPRANE® nor fresh pineapple
Batch n°2: DOLIPRANE® on the basis of 2 g/kg of live weight (LW) per day for 2 weeks, then fresh pineapple on the basis of 13 mg/kg of LW per day for 4 weeks
Batch n°3: DOLIPRANE® at the rate of 2 g/kg of LW per day for 2 weeks, then fresh pineapple at the rate of 26 mg/kg of LW for 4 weeks
Batch n°4: DOLIPRANE® on the basis of 2 g/kg of LW per day for 2 weeks and without any treatment by fresh pineapple.

Table 2. Level of glutamate pyruvate transaminase (GPT).

Batches	Glutamate Pyruvate Transaminase in UI/L		
	J0	**J14**	J42
Batch n°1	69,33±0,88 a	70,33±0,88 a	61,67±10,41 a
Batch n°2	70,33±1,67 a	242,67±31,67 b	106±2,31 c
Batch n°3	70,67±4,25 a	248,67±35,89 b	118,33±11,67 c
Batch n°4	73±1,53 a	286,33±3,18 c	295±2,64 b
Probability	**0,75 ns**	**0,0009*** **	**<0,0001*** **

*** Very highly significant difference on the threshold of 0.1%
Ns non significant difference on the threshold of 5%. Average values followed by the same letter are non-significantly different on the threshold of 5% probability. Those followed different letters are significantly different**.**
Batch n°1: control batch, neither DOLIPRANE® nor fresh pineapple
Batch n°2: DOLIPRANE® on the basis of 2 g/kg of live weight (LW) per day for 2 weeks, then fresh pineapple on the basis of 13 mg/kg of LW per day for 4 weeks
Batch n°3: DOLIPRANE® at the rate of 2 g/kg of LW per day for 2 weeks, then fresh pineapple at the rate of 26 mg/kg of LW for 4 weeks
Batch n°4: DOLIPRANE® on the basis of 2 g/kg of LW per day for 2 weeks and without any treatment by fresh pineapple.

Table 3. Level of glutamate oxaloacetic transaminase (GOT).

Batches	Glutamate oxaloacetic transaminase in UI/L		
	J0	**J14**	J42
Batch n°1	41±3,05 a	45,67±2,33 a	47,33±6,84 a
Batch n°2	47,33±4,37 a	184,67±3,75 b	117,33±2,73 c
Batch n°3	47,68±3,38 a	181±5,51 b	114,67±4,83 c
Batch n°4	43,33±2,40 a	171±3,78 c	178±1,53 b
Probability	**0,75 ns**	**0,0009*** **	**<0,0001*** **

*** Very highly significant difference on the threshold of 0.1%
Ns non significant difference on the threshold of 5%. Average values followed by the same letter are non-significantly different on the threshold of 5% probability. Those followed different letters are significantly different**.**
Batch n°1: control batch, neither DOLIPRANE® nor fresh pineapple
Batch n°2: DOLIPRANE® on the basis of 2g/kg of live weight (LW) per day for 2 weeks, then fresh pineapple on the basis of 13 mg/kg of LW per day for 4 weeks
Batch n°3: DOLIPRANE® at the rate of 2g/kg of LW per day for 2 weeks, then fresh pineapple at the rate of 26mg/kg of LW for 4 weeks
Batch n°4: DOLIPRANE® on the basis of 2g/kg of LW per day for 2 weeks and without any treatment by fresh pineapple.

the threshold of 5%. Following the intoxication with DOLIPRANE®, a significant difference was noticed between batch n°1 and the three other batches on the threshold of 0.1%, on J14. At the end of the experimenttation, the values of batches n° 2 and n°3 significantly decreased in comparison with J14, but couldn't reach the level of batch n° 1(Table 3).

DISCUSSION

Evolution of alkaline phosphatase (ALP)

The serum concentrations in UI/L concerning alkaline phosphatase among the rats in batch n° 1 all the experimentation long and among the rats of the other three batches on J0 are regarded as physiological values for that simple of rats. Those values are not in concordance with the ones measured by (Kaneko, 1989). As a matter of fact, the ALP normal plasma value established.

By that author was 419 ± 15, but this concerns female rats. The fact that age and sex can influence the serum level of the alkaline phosphatase accounts for that difference (Rousseau, 1978).

The alkaline phosphatase level globally increased among all the rats following intoxication by DOLIPRANE®. The increase in that enzyme serum level has

already been pointed out by Rousseau (1978) in relation to liver alterations, especially when there are liver mechanical disturbances which result in a stasis of the liver. As the enzyme can no longer be normally eliminated by the bile, it is therefore reabsorbed and passes through blood. Thus, in case of icteria due to bile retention, it is noticed an increase in that enzyme rate in the serum. It is probable that this increase is proportional to the obstruction degree of the biliary tubes.

Following the treatment with pineapple, the alkaline Phosphatase levels respectively dropped from 406.67 ± 7.17 UI/L to 223.67 ± 3.71 UI/L regarding batch n°2 and from 408.33 ± 2.03UI/L to 222.67 ± 3.71UI/L regarding batch n°3. The positive impact of fresh pineapple upon the liver of the rats previously intoxicated by praracetamol could account for that significant decrease. Indeed, fresh pineapple contains, according to Schulz et al., (2001), a mixture of digestive enzymes the most important of which is bromelaine.

That enzyme is absorbed by the organism and passes through the blood to fulfil a systemic activity. Thus, it inhibits the production of prostaglandins which provoke inflammations (Stone et al., 2002).

The decrease in inflammatory phenomenon results in the retrogression of liver deteriorations, hence the fall in ALP serum concentration among the wistar rats first intoxicated then treated.

Evolution of glutamate pyruvate transaminase (GPT)

The GPT values, 74.7 ± 3.8 UI/L are in concordance with those defined by Kamdem et al., (1981) but significantly differ from those established by (Vaissaire, 1989).

In fact, the latter had proposed 130 UI/L as the GPT average value among three-months old rats whereas the rats used in the present experimentation are five months old. Therefore, muscle exercise is likely to change the GPT plasma level (Lecoanet, 1981). Following the intoxication, the GPT levels considerably increased as far as batches 2, 3 and 4 were concerned. As that enzyme is located in several tissues, mainly in the liver, the heart and the skeleton muscles, the increase in its values due to the use of DOLIPRANE® would lead to those organs malfunction. For instance, as regards severe viral or medicinal hepatitis, rates from 500 to 1500 UI/L have been noticed among men. Besides, an ischemic hepatic developing along with a severe toxic necrosis or a serious hypoxia displays values superior to 3000UI/L (Scheurer et al., 2002).

Levels of glutamate oxaloacetic transaminase (GOT)

The obtained GOT normal values differ from those 178 ± 20.99 UI/L and 200 ± 26 UI/L respectively proposed by Kamdem et al., (1981) and Vaissaire (1989). On the other hand, those results are in harmony with the value 42.9 ± 10.1 UI/L established by Kaneko (1989). In those cases; the age factor is also incriminated. The intoxication with DOLIPRANE® made the GOT rate increase in batches 2, 3 and 4. That enzyme is found out in several tissues: liver, heart, kidney, muscles spleen and intestine; therefore, it is not specific to a particular organ, but its activity is more important in the liver, the heart and the muscles (Schünck and Alain, 1997). The increase in the GOT plasma rate following the intoxication by DOLIPRANE® could have been caused by a malfunction of those organs especially at the level of the liver. In fact, it is probable that the increase in the GOT activity is constant among men suffering from a severe hepatitis (Rousseau, 1978). In addition, Banting et al. (1975) emphasize that the increase in the GOT rate is a sign of tissue necrosis, more particularly a hepatic one. Lecoanet (1981) also stresses that, among cattle and sheep, the GOT plasma values undergo an important increase during acute liver ailments. It is less pronounced during chronic hepatitis**.** Thus, liver abscesses do not often significantly modify the GOT and the GPT activity, since the exploration of those two enzymes is often carried out in a coupled way. When the GOT is high and the GPT is normal, a muscle attack is suspected; if the GOT and the GPT increase simultaneously, a liver attack is suspected (Lecoanet, 1981).

In the present study, the results establish the increase in those two enzymes, which confirms a liver attack.

On the whole, the use of fresh pineapple made the ALP, GPT and GOT rates decrease among the rates in batches 2 and 3, through the normal values were not found out. Anatomopathological and histopatological tests which were carried out on the liver of the very rats confirm that effectiveness (Dougnon and Kpodékon, 2006).

Conclusion

This study confirms the effectiveness of pineapple in the control of liver malfunctions among wistar rats intoxicated with paracetamol. However, it is desirable that other biological or biochemical parameters related to liver attack be explored so that the obtained results can be supported.

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