

Synergic Effect of Herbicides Formulation on Energy Compounds and Myokinase Activity of Albino Rats Organs

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Abstract

The present work evaluate the effects of single and multi doses of glyphosate and fluazifop-butyl as herbicides in pure and formulated forms on the energetic compounds and myokinase activity in the organs of albino rats. The results indicated the following remarks:

The single dose showed an increase in ATP content in all investigated rat organs by both herbicides ingestion. However, the increase induced by formulated herbicides was more clear than those of pure ones. In contrast, the levels of ADP and AMP were decreased vigorously under the herbicides ingestion. The decrease caused by formulated herbicides was higher than that of the pure ones. Herbicides exhibited a remarkable inhibition in myokinase activity in all examined rat organs relative to control. The inhibition caused by formulated herbicides was more obvious than those of pure herbicides.

The results showed that, the effects of multi doses of herbicides were similar to the influence of the single dose in all items such as ATP, ADP, AMP contents and myokinase activity. However, these effects were more than that of single dose. The influence of the formulated herbicides was more obvious (toxic) than the pure ones .

Introduction

To establish any toxicological data acute toxicity tests are considered the base line or preliminary studies for chronic toxicity tests. In this respect, glyphosate and fluazifop-butyl are commonly used in Egypt. It should be emphasized that no or very little data are available in the literature about this influence of pure and formulated herbicides on different living organisms and human health.

In developing countries, the use of pesticides has become so important that their use is inextricably linked with improvement of human welfare (Osibajo, 1989). Pesticides are usually applied in their formulated form where the active ingredient is combined with organic solvents, emulsifying and wetting agents, which affect the pesticides penetration. The formulations way cause synergism or antagonism to the toxicity of the active ingredient (El-Sebae, 1985). Recently, the W.H.O. (1991) emphasized that the final toxic classification of any pesticide in intended to be by its formulation. Indeed, literature background revealed that a few reports dealt with the metabolic changes and with other side effects of formulated herbicides as compared with pure one. Abou-Zeid et al., (1993) observed that formulated malathion was more toxic to

rats than that of the pure technical ingredient, and blood serum profile was changed by formulated malathion more than that by pure one with dermal treatment.

In this respect, Abdel-Rahim et al (1994e) and Knopp and Glass (1997) reported that organs tissue contents of adenosine-5-phosphate (ATP) were increased, whereas the contents of adenosine-5-diphosphate (ADP) and adenosine-5-monophosphate (AMP) were decreased and accompanied by inhibiting the activity of myokinase either under the effect of pure or formulated herbicides of all tested organs, relative to control.

In the present study, pure herbicides and formulated ones in single and multi doses were administered separately in dose of 1/20 from LD₅₀ every 48 hours to adult albino rats. The effect of these doses on the energetic compounds ATP, ADP, AMP, and myokinase were investigated.

Materials and Methods

Herbicides:

Two herbicides were used; the first one is known as Glyphosate (N-(phosphonomethyl)glycine); belongs to organophosphorous family, non-selective systemic herbicide, acts on various enzyme systems, thus interfering with the formation of amino acids and other important endogenous chemicals. Second one is known as Fluazifop-butyle (butyl(RS)-2-(4-(5-trifluoromethyl-12-pyridyloxy)phenoxy)propionate); belongs to phenoxy, trifluoromethyl and pyridine family; selective systemic herbicide, acts by interfering with ATP production (Agrochemicals Handbook, 1987). The herbicides were obtained from Katou Jonker, Denmark, and was provided from the central Agricultural Pesticide Laboratory, ARC, Ministry of Agriculture, Dokki, Egypt.

Experimental Animals:

A total of 45 adult male albino rats weighing 100-120 g were used in the present study and raised in the animal house of the Biochemistry Department, Faculty of Agriculture; Cairo University. The albino rats were kept under normal laboratory conditions for two weeks before the comencing of the experiments. The animal were allowed free access of water and fed on a uniformly basal diet for a period of three months and were orally administrated herbicides at one single dose of 1/4 from LD₅₀ and multi doses of 1/20 from LD₅₀ every two days as follows:

Group(1) control, untreated.

Group (2) rats administrated pure glyphosate at a dose of 165 mg/Kg b.w.

Group (3) rats administrated formulated glyphosate at a dose of 330 mg/Kg b.w.

Group(4) rats administrated pure fluazifop-butyl at 280 mg/Kg b.w.

Group (5) rats administrated formulated fluazifop-butyl at 560 mg/Kg body weight.

The animals were killed by decapitation after 2 days of the last induction, then liver, brain, spleen, kidney and hearts were dissected out.

Chemical Analysis:

A spectrophotometric method was used for the determination of ATP, ADP and AMP in the rat organs homogenates using a Pye Unicam spectrophotometer (Model Sp 1800), where ATP was determined according to Lamprecht and Trauschold (1962) and ADP and AMP were determined as described by Adams (1962). The activity of myokinase in the rat organs homogenates was also spectrophotometrically measured as reported by Bergmeyer (1974).

Statistical Analysis:

The obtained data were statistically analyzed using the method of Kalton (1967). The probability was determined by reference to (t) distribution table probability at 0.05 and used as a point of significance according to Bailay (1955).

Results**A- Single Dose:****A-1- Herbicidal Effect on ATP, ADP, and AMP Contents :**

After two days of ATP, ADP and AMP were determined in different rat organ tissues. The results are shown in **Tables 1, 2 and 3**.

A significant decrease in the ADP and AMP contents in all investigated organs by herbicides induction was noticed. On the other hand, ATP showed an opposite trend where an increase in ATP level was encountered under herbicides application (**Table 1**). The ATP levels were increased by 20.00%, 26.67%, 13.33% and 22.67% for brain; 13.64%, 18.18%, 10.91% and 19.09% for liver; 12.50%, 25.00%, 17.50% and 17.50% for spleen; 15.00%, 50.00%, 15.00% and 50.00% for kidneys and 9.80%, 17.65%, 13.73 and 17.65% for heart relative to control under the ingestion of pure and formulated glyphosate and fluazifop-butyl, respectively.

On the other hand, the ADP levels (**Table 2**) were decreased by 21.54%, 36.92%, 23.08% and 35.38% for brain; 33.33%, 46.67%, 26.67% and 53.33% for liver; 13.64%, 22.73%, 18.18% and 22.73% for spleen; 37.50%, 43.75%, 31.25% and 50.00% for kidneys and 15.00%, 20.00%, 20.00% and 25.00% for heart than control under the effect of pure and formulated glyphosate and fluazifop-butyl, respectively.

In connection with AMP (**Table 3**), its levels were reduced than control by 35.48%, 41.94%, 32.26% and 38.71% for brain; 17.81%, 30.14%, 21.92% and 30.14% for liver; 14.29%, 22.86%, 17.14% and 25.71% for spleen; 13.64%, 22.73%, 18.18% and 22.73% for kidneys and 25.00%, 45.00%, 30.00% and 40.00% for heart, respectively after the administration of pure and formulated glyphosate and fluazifop-butyl.

A-2- Herbicidal Effect on Myokinase Activity :

The myokinase activity were determined in the various organ tissues after herbicides administration to rats and the results are shown in **Table 4**. The results indicated that herbicides caused a remarkable decrease in myokinase activity of all organs tissues. The decreased values were 31.91%, 40.43%, 27.66% and 40.43% for brain; 33.33%, 46.67%, 31.11% and 37.78% for liver; 20.00%, 37.14%, 17.14% and 34.29% for spleen, 35.00%, 45.00%, 30.00% and 30.00% for kidneys and 20.00%, 25.00%, 22.50% and 25.00% for heart relative to control respectively under the effect of pure and formulated glyphosate and fluazifop-butyl.

Table (1): Effect of herbicides single dose on ATP level in different organs of albino rats.

Organ		Control	Glyphosate		Fluazifop-butyl	
			Pure	Formulated	Pure	Formulated
Brain	*	7.5 ± 0.8 a	9.0 ± 0.8 b	9.5 ± 0.8 b	8.5 ± 0.6 b	9.2 ± 1.0 bc
	%	100.00	120.00	126.67	113.33	122.67
Liver	*	11.0 ± 1.0 a	12.5 ± 1.01 b	13.0 ± 1.1 b	12.2 ± 1.2 b	13.1 ± 1.2 bc
	%	100.00	113.64	118.18	110.91	119.09
Spleen	*	4.0 ± 0.3 a	4.5 ± 0.5 b	5.0 ± 0.4 bc	4.7 ± 0.5 b	4.7 ± 0.5 b
	%	100.00	112.50	125.00	117.50	117.50
Kidneys	*	2.0 ± 0.2 a	2.3 ± 0.3 b	3.0 ± 0.2 bc	2.3 ± 0.2 b	3.0 ± 0.3 bc
	%	100.00	115.00	150.00	115.00	150.00
Heart	*	5.1 ± 0.5 a	5.6 ± 0.6 b	6.0 ± 0.5 b	5.8 ± 0.6 b	6.0 ± 0.6 b
	%	100.00	109.80	117.65	113.73	117.65

The numbers in the row followed by the same letter are not significantly different at P = 0.05 for each parameter. * = µM/g tissue

Table (2): Effect of herbicides single dose on ADP level in different organs of albino rats.

Organ		Control	Glyphosate		Fluazifop-butyl	
			Pure	Formulated	Pure	Formulated
Brain	*	0.65 ± 0.07 a	0.51 ± 0.06 b	0.41 ± 0.04 b	0.50 ± 0.04 b	0.42 ± 0.04 bc
	%	100.00	78.46	63.08	76.92	64.62
Liver	*	0.15 ± 0.01 a	0.10 ± 1.01 b	0.08 ± 0.01 bc	0.11 ± 0.10 b	0.07 ± 0.01 bc
	%	100.00	66.67	53.33	73.33	46.67
Spleen	*	0.22 ± 0.02 a	0.19 ± 0.02 b	0.17 ± 0.02 b	0.18 ± 0.01b	0.17 ± 0.02 b
	%	100.00	86.36	77.27	81.82	77.27
Kidneys	*	0.16 ± 0.02 a	0.10 ± 0.01 b	0.09 ± 0.01 bc	0.11 ± 0.01 b	0.08 ± 0.01 bc
	%	100.00	62.50	56.25	68.78	50.00
Heart	*	0.20 ± 0.02 a	0.17 ± 0.02 b	0.16 ± 0.01 b	0.16 ± 0.02 b	0.15 ± 0.01 b
	%	100.00	85.00	80.00	80.00	75.00

The numbers in the row followed by the same letter are not significantly different at P = 0.05 for each parameter. * = µM/g tissue

Table (3): Effect of herbicides single dose on AMP level in different organs of albino rats.

Organ		Control	Glyphosate		Fluazifop-butyl	
			Pure	Formulated	Pure	Formulated
Brain	*	0.31 ± 0.03 a	0.20 ± 0.02 b	0.18 ± 0.02 b	0.21 ± 0.01 b	0.19 ± 0.02b
	%	100.00	64.52	58.86	67.74	61.29
Liver	*	0.73 ± 0.07 a	0.60 ± 0.0 b	0.51 ± 0.05 bc	0.57 ± 0.06 b	0.51 ± 0.05 bc
	%	100.00	82.19	69.86	78.08	69.86
Spleen	*	0.35 ± 0.03 a	0.30 ± 0.02 b	0.27 ± 0.03 b	0.29 ± 0.03 b	0.26 ± 0.02 bc
	%	100.00	86.71	77.14	82.86	74.29
Kidneys	*	0.22 ± 0.01 a	0.19 ± 0.02 b	0.17 ± 0.02 bc	0.18 ± 0.01 b	0.17 ± 0.02 b
	%	100.00	86.36	77.27	81.82	77.27
Heart	*	0.40 ± 0.03 a	0.30 ± 0.03 b	0.22 ± 0.02 bc	0.28 ± 0.03 b	0.24 ± 0.02 bc
	%	100.00	75.00	55.00	70.00	60.00

The numbers in the row followed by the same letter are not significantly different at P = 0.05 for each parameter. * = µM/g tissue

Table (4): Effect of herbicides single dose on Myokinase level in different organs of albino rats.

Organ		Control	Glyphosate		Fluazifop-butyl	
			Pure	Formulated	Pure	Formulated
Brain	*	0.47 ± 0.05 a	0.32 ± 0.03 b	0.28 ± 0.03 bc	0.34 ± 0.04 b	0.28 ± 0.02 bc
	%	100.00	68.09	59.57	72.37	59.57
Liver	*	0.45 ± 0.05 a	0.30 ± 0.02 b	0.24 ± 0.02 bc	0.31 ± 0.03 b	0.28 ± 0.03b
	%	100.00	66.67	53.33	68.89	62.22
Spleen	*	0.35 ± 0.04	0.28 ± 0.03 b	0.22 ± 0.02 bc	0.29 ± 0.03 b	0.23 ± 0.02 bc
	%	100.00	80.00	62.86	82.86	65.71
Kidneys	*	0.20 ± 0.01 a	0.13 ± 0.01b	0.11 ± 0.01 bc	0.14 ± 0.01 b	0.14 ± 0.01 b
	%	100.00	65.00	55.00	70.00	70.00
Heart	*	0.40 ± 0.03 a	0.32 ± 0.03 b	0.30 ± 0.03 b	0.31 ± 0.03 b	0.30 ± 0.03 b
	%	100.00	80.00	75.00	77.50	75.00

The numbers in the row followed by the same letter are not significantly different at P = 0.05 for each parameter.

* = $\mu\text{M}/\text{mg}$ protein.

B- Multi doses:

B-1- Herbicidal Effect on the Levels ATP, ADP and AMP:

In this respect, the levels of ATP, ADP and AMP in different organs were determined and the data were presented in **Tables 5, 6 and 7**. The results illustrated that the ATP content (**Table 5**) of herbicides induced rat organs was higher than that of control. The levels were 33.33%, 46.67%, 33.33%, and 33.33% for brain; 18.18%, 27.27%, 13.64% and 27.27% for liver; 17.95%, 28.21%, 15.38 and 28.21% for spleen; 20.00%, 25.00%, 25.00% and 25.00% for kidneys, and 14.00%, 20.00%, 16.00% and 20.00% for heart relative to control under the effect of pure and formulated glyphosate and fluazifop-butyl, respectively. Generally speaking, the formulated and pure herbicides under study possessed the same effect on ATP level of rats.

ADP and AMP contents were decreased in all rat organs than control after the herbicides induction period. The ADP decreased values than control (**Table 6**) were 24.24%, 31.82%, 22.73% and 28.79% for brain; 37.50%, 37.50%, 43.75% and 31.25% for liver; 17.39%, 30.43%, 13.04% and 21.74% for spleen; 33.33%, 53.33%, 40.00% and 46.67% for kidneys, and 19.05%, 28.57%, 19.05% and 28.57% for heart relative to control under the effect of pure and formulated glyphosate and fluazifop-butyl, respectively.

On the other hand, the decreased values than control of AMP (**Table 7**) were 30.00%, 40.00%, 36.67% and 36.67% for brain; 20.27%, 32.43%, 17.57% and 25.68% for liver; 14.29%, 22.86%, 11.43% and 20.00% for spleen; 17.39%, 30.43%, 13.04% and 30.43% for kidneys, and 29.27%, 51.22%, 24.39% and 46.34% for heart relative to control. Here again, the pure and formulated herbicides caused the same effect on the levels of energy compounds in most cases.

B-2- Herbicidal Effect on Myokinase Activity:

After the herbicides induction, myokinase activity was determined in brain, liver, spleen, kidneys and heart; and the results are shown in **Table (8)**. A remarkable decrease was observed in myokinase activity in all investigated organs by the herbicides induction. The decreased values than control were 37.50%, 43.75%, 27.08% and 37.50% for brain; 36.96%, 41.30%, 30.43% and 36.96% for liver; 22.22%, 41.67%, 13.89% and 30.56% for spleen; 38.10%, 52.38%, 39.10% and 47.62% for kidneys, and 25.00%, 25.00%, 20.00% and 25.00% for heart relative to control under the effect

of pure and formulated glyphosate and fluazifop-butyl, respectively. Once again, the pure and formulated herbicides under study possessed the same effect on myokinase activity in most cases.

Table (5): Effect of herbicides single doses on ATP level in different organs of albino rats.

Organ		Control	Glyphosate		Fluazifop-butyl	
			Pure	Formulated	Pure	Formulated
Brain	*	7.5 ± 0.6 a	10.0 ± 1.0 b	11.0 ± 1.1 bc	9.5 ± 0.9 b	1.0 ± 7.5 b
	%	100.00	133.335	146.67	126.67	133.33
Liver	*	11.0 ± 1.0 a	13.0 ± 0.9 b	14.0 ± 1.3 b	12.5 ± 1.2 b	14.0 ± 1.3 bc
	%	100.00	118.18	127.27	113.64	127.27
Spleen	*	3.9 ± 0.4 a	4.6 ± 0.5 b	5.0 ± 0.4 bc	4.5 ± 0.4 b	5.0 ± 0.4 bc
	%	100.00	117.95	128.21	115.38	128.21
Kidneys	*	2.0 ± 0.2 a	2.4 ± 0.2 b	2.0 ± 0.3 b	2.5 ± 0.1 b	2.5 ± 0.2 b
	%	100.00	120.00	125.00	125.00	125.00
Heart	*	5.0 ± 0.5 a	5.7 ± 0.6 b	6.0 ± 0.5 b	5.8 ± 0.5 b	6.0 ± 0.5 b
	%	100.00	114.00	120.00	116.00	120.00

The numbers in the row followed by the same letter are not significantly different at P = 0.05 for each parameter.

* = $\mu\text{M/g}$ tissue.

Table (6): Effect of herbicides multi doses on ADP level in different organs of albino rats.

Organ		Control	Glyphosate		Fluazifop-butyl	
			Pure	Formulated	Pure	Formulated
Brain	*	0.66 ± 0.06 a	0.50 ± 0.04 b	0.54 ± 0.05 b	0.51 ± 0.04 b	0.47 ± 0.05 b
	%	100.00	75.765	68.18	77.27	71.21
Liver	*	0.16 ± 0.01 a	0.10 ± 0.01 b	0.10 ± 0.01 b	0.09 ± 0.01 b	0.11 ± 0.01 b
	%	100.00	62.50	62.50	56.25	68.75
Spleen	*	0.23 ± 0.02 a	0.19 ± 0.02 b	0.16 ± 0.01 bc	0.20 ± 0.02 b	0.18 ± 0.02 b
	%	100.00	82.61	69.57	86.96	68.75
Kidneys	*	0.15 ± 0.01 a	0.10 ± 0.01 b	0.07 ± 0.01 bc	0.09 ± 0.01 b	0.18 ± 0.02 b
	%	100.00	66.67	46.67	60.00	78.26
Heart	*	0.21 ± 0.02 a	0.17 ± 0.02 b	0.15 ± 0.01 b	0.17 ± 0.01 b	0.08 ± 0.01 b
	%	100.00	80.95	71.43	80.95	71.43

The numbers in the row followed by the same letter are not significantly different at P = 0.05 for each parameter.

* = $\mu\text{M/g}$ tissue

Table (7): Effect of herbicides multi doses on AMP level in different organs of albino rats.

Organ		Control	Glyphosate		Fluazifop-butyl	
			Pure	Formulated	Pure	Formulated
Brain	*	0.30 ± 0.02 a	0.21 ± 0.02 b	0.18 ± 0.08 bc	0.19 ± 0.001 b	1.19 ± 0.01 b
	%	100.00	70.05	60.00	63.33	63.33
Liver	*	0.74 ± 0.07 a	0.59 ± 0.06 b	0.50 ± 0.05 bc	0.61 ± 0.05 b	0.55 ± 0.05 b
	%	100.00	79.73	67.57	82.43	74.32
Spleen	*	0.35 ± 0.04 a	0.30 ± 0.02 b	0.27 ± 0.02 b	0.31 ± 0.02 b	0.28 ± 0.02 b
	%	100.00	85.71	77.41	88.57	80.00
Kidneys	*	0.23 ± 0.02 a	0.19 ± 0.02 b	0.16 ± 0.01 bc	0.20 ± 0.02 b	0.16 ± 0.01 bc
	%	100.00	82.61	69.57	86.96	69.57
Heart	*	0.41 ± 0.04 a	0.29 ± 0.03 b	0.20 ± 0.02 bc	0.31 ± 0.03 b	0.22 ± 0.02 bc
	%	100.00	70.73	84.78	75.61	53.66

The numbers in the row followed by the same letter are not significantly different at P = 0.05 for each parameter.

* = $\mu\text{M/g}$ tissue

Table (8): Effect of herbicides multi doses on Myokinase level in different organs of albino rats.

Organ		Control	Glyphosate		Fluazifop-butyl	
			Pure	Formulated	Pure	Formulated
Brain	*	0.48 ± 0.05 a	0.30 ± 0.03 b	0.27 ± 0.03 b	0.35 ± 0.03 b	0.30 ± 0.02 bc
	%	100.00	62.505	56.25	72.92	62.50
Liver	*	0.46 ± 0.04 a	0.29 ± 0.03 b	0.27 ± 0.03 b	0.32 ± 0.03 b	0.29 ± 0.03 b
	%	100.00	63.04	58.70	69.57	63.04
Spleen	*	0.36 ± 0.04 a	0.28 ± 0.02 b	0.21 ± 0.02 bc	0.31 ± 0.03 b	0.25 ± 0.02 bc
	%	100.00	77.78	58.33	86.11	69.44
Kidneys	*	0.21 ± 0.02 a	0.13 ± 0.01 b	0.10 ± 0.01 bc	0.13 ± 0.01 b	0.11 ± 0.01 b
	%	100.00	61.90	47.62	61.90	52.38
Heart	*	0.40 ± 0.03 a	0.30 ± 0.03 b	0.30 ± 0.02 b	0.32 ± 0.03 b	0.30 ± 0.02 b
	%	100.00	75.00	75.00	80.00	75.00

The numbers in the row followed by the same letter are not significantly different at P = 0.05 for each parameter.

* = $\mu\text{M}/\text{mg}$ protein

Discussion

A- Herbicidal Effect on The Energy Compounds :

Adenosine-5-triphosphate (ATP), adenosine-5-diphosphate (ADP) and adenosine-5-phosphate (AMP) were determined in different organ tissues of induced rats. A remarkable decrease was observed in ADP and AMP contents. In contrast, ATP content was increased in all investigated organs by herbicides ingestion.

The significant effects of the investigated herbicides on the different organs are summarized in **Table (9)**.

These results might be related either to the high rate of ATP synthesis or the energy liberated during the metabolic processes through trapping inorganic phosphate with AMP and ADP to form ATP. These findings were in parallel with the results of Abdel-Rahim et al., (1994e) and Knopp and Glass (1997).

The results of ATP, ADP and AMP led to suggest that at any circumstances associated with diminished availability of the prime dietary source of energy, namely carbohydrate, will accentuate utilization of fatty acids for this purpose. In this respect, the stimulation of glycolytic metabolism (forms pyruvic acids and then acetyl CoA) led to accumulate ATP and creatinine stores (Lehninger, 1982 and Abdel-Rahim et al, 1994b). ATP is rapidly utilized in protein biosynthesis through converting to cAMP which stimulated by the adenylate cyclase (Adams et al, 1993).

B- Herbicidal Effect on Myokinase Activity:

After herbicides ingestion the myokinase activity was determined in different organs tissues of rats and a remarkable decrease in the myokinase activity was noticed in all tissues relative to control.

In general, the increase in ATP level after herbicides ingestion was mainly due to the effect of herbicides on the respiratory system. The maintenance of tissues energy is likely accomplished through increase the glycolysis process. Accordingly, an inhibition in LDH activity caused an increase of energy utilization for tissue processes (Abdel-Rahim et al, 1994b).

The tight coupling of oxidation to phosphorylation, provided a means by which the role of oxidation of food stuffs by respiratory oxygen. The utilization of ATP to drive the divers energy requiring processes of the cells automatically increased the available supply of ADP and inorganic phosphate, which in turn become available to react in the

coupling mechanism and permit respiration to proceed. In the herbicides ingestion condition, the oxidative phosphorylation was stimulated due to the respiration oxygen and the increase of ATP formation (Lehninger, 1982).

Myokinase catalyzes the conversion of 2 molecules of ADP to one molecule of each of ATP and AMP through the following reaction:



This reaction was observed after the complete utilization of ATP. The higher level of ADP than AMP might be due to the utilization of high amounts of ATP in metabolic processes and was converted to ADP (Lehninger, 1982).

The results of the present work emphasized that an urgent rules are needed for global regulation to impose legislation and guidelines for registration and handling of agro-chemical including pesticides which have direct access to the food chain, ought to include methodologies and laboratory facilities for their implementation in many of the developing countries.

Table (9): The influence of Glyphosate and Fluazifop[-butyl on rat organs parameters.

Parameters	Glyphosate		Fluazifop[-butyl	
	Pure	Formulated	Pure	Formulated
Heart parameters				
ATP level	+	++	+	+
ADP	-	-	-	-
ADP	-	--	-	--
Myokinase	-	-	-	-
Kidneys parameters				
ATP level	+	++	+	++
ADP	-	--	-	--
ADP	-	--	-	-
Myokinase	-	--	-	-
Spleen parameters				
ATP level	+	++	+	+
ADP	-	-	-	-
ADP	-	--	-	--
Myokinase	-	-	-	--
Brain parameters				
ATP level	+	++	+	++
ADP	-	-	-	--
ADP	-	-	-	-
Myokinase	-	--	-	--
Liver parameters				
ATP level	+	+	+	++
ADP	-	--	-	--
ADP	-	--	-	-
Myokinase	-	-	-	-

The symbols (+, -) and (++, --) indicates significant and highly significant increase or decrease, respectively relative to control rats group.

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