STUDY ON THE IMPACT OF METFORMIN ON THE EFFECT OF PALM OIL IN THE METABOLISM OF CARBOHYDRATES

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Introduction: Research has been published on the frequency of Metformin use in patients with various complications who have been using fat-rich foods. Our analysis of a large number of studies shows that: in parallel with the improvement of the function of the liver, insulin resistance is also improved. In the recent years, studies have been conducted on the impact of Metformin mechanisms on the insulin resistance.

Purpose of the Presentation: the attempt to study the impact of Metformin on the laboratory mice, treated for a longer period of time, continuously with palm oil.

Materials and Methods: experiments were conducted on adult male mice, divided into 4 groups, each group with 5-6 experimental animals. Palm oil and Metforminwas applied per os. The period between palm oil and metformin appliance was 4-5 hours of difference. The experiments were carried out at the Medical University of Sofia, at the Scientific Research Laboratory of the Department of Pharmacology and Toxicology

Results: Figure 1 shows significant statistical differences between the research group with palm oil and the research groupwith palm oil + Metformin, on the 60th day of the study. The continuation of Metformin's admission along with the palm oil reduces body weight gain of the experimental animals. Figure 2 shows the results of TTG (Glucose Tolerance Test).The analysis of these data shows that, under the influence of palm oil, prediabetes is developed. However, under the influence of Metformin, this condition of prediabetes is prevented. This can be seen from the results of the use of palm oil + the group treated with Metformin. Figure 3 shows the results of the determination of INF-γ on the 30th and 60th dayof the experiments on the adult animals. The results show that palm oil reduces the level of interferon gamma. Metformin antagonizes the suppressive effect of palm oil in the interferon gamma.

Key words: insulin resistance, palm oil, Metformin

INTRODUCTION

Research has been published on the frequency of metformin use in patients with various complications from the use of fat-rich foods. (Angelico et al., 2007) published studies that document the results of ten clinical studies, during which metformin has improved hepatocytesfunction in patients with cirrhosis, lipodystrophy, hepatitis (all non-alcoholic fatty liver diseases). Our analysis of a large number of studies shows that, in parallel with the correction of black liver function, insulin resistance is also improved. In recent years, metformin's mechanisms of action against insulin resistance have been studied. There is no published data on the study of the metformin effect on palm oil influence and carbohydrate metabolism indicators.

2. Purpose of presentation

Attempting to study the impact of metformin on experimental mice, which we treated for a long time, consistently with palm oil.

3. Materials and Methods

Efforts were made on adult male mice, divided into 4 groups, each group with 5-6 experimental animals.

First group: controlling

Second group: Experimental with palm oil – the animals were treated with palm oil for up to 60 days, once a day with a dose of 1ml/100 grams.

Third group: Experimental with metformin. The animals were treated for 30 days with metformin, once daily with a dose of 100mg/kg orally.

Fourth group: Experimental: animals were treated in combination with palm oil (1ml/100g) + metformin (100mg/kg per day).

The experiments were carried out at the State Medical University in Sofia, at the Department of Pharmacology and Toxicology Research Laboratory.

Both substances were applied per os, the period between palm oil and metformin application was 4-5 hours difference. Metforminwas introduced 30 days after we applied palm oil based on the results we had previously presented in other works with data on the presentation of changes in fats and carbohydrates, after 30 days of palm oil treatment. (Animals from Group 4 were treated with 60 days of palm oil and the last 30 days with metformin).

RESULTS

Figure 1 shows the results from the determination of body weight of experimental animals. Significant statistical differences were found between the palm oil and palm oil + metformin group on the 60th day of the study.

The continuation of Metformin during palm oil treatment reduces the weight gain of the experimental animals. The tendency of the reduction of the total mass under the influence of Metformin is also observed during the comparison with the control group.
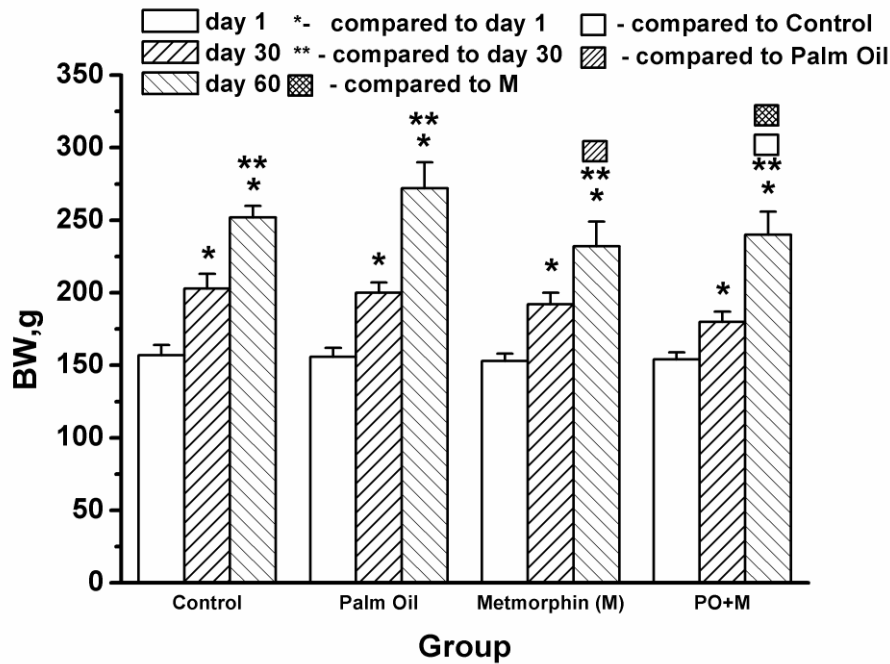
Figure 1. Influence of palm oil and metformin on the body weight of large experimental mice (60-day chronological research)
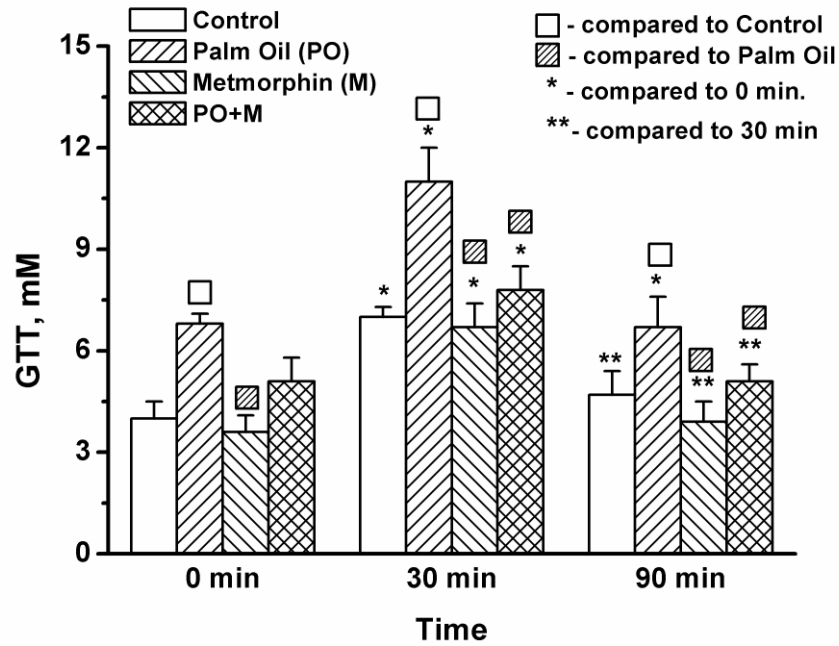
Statistical analysis

ONE-WAYANOVA: P<0.0001; Bartlett: SD's belong to the same population; Bonferoni t critical=3.583.

Discussion

Statistically important is the increase in body weight in three experimental animal groups. The 60-day study results show statistically significant differences as follows:

1. The combination of palm oil + metformin changes the statistically significant weight with the control group (P <0.001) and in comparison to the metformin-treated group (P <0.001).
2. The weight of experimental animals treated with metformin differs from that of the animal weight, treated with palm oil

Figure 2 shows the results of the conducted GTT (Glucose Tolerance Test). The analysis of these data shows that under the influence of palm oil, prediabetes is developed. Statistically significant are changes in the 90th minute by the glucose loading test between the control group and those treated with palm oil for 60 days. Under the influence of metformin, prediabetes is prevented, which can be seen from the results of palm oil + metformin-treated group. The results show narrow blood sugar curves of the control group's animals. Metformin self-administration is associated with GTT results, close to those of the control group.

Figure 2. The effect of palm oil and metformin on insulin resistance of adult animals from the Wistar line.

Statistical analysis

One Way ANOVA: P<0.0001; Bartlett: SD's belong to the same poplation; Bonferoni: critical t=3.598

Discussion

The results of this study confirm the above data that the continuous intake of palm oil results in an increase in blood glucose in all measurements parallel to the control group (P <0.001 for the three values measured at 0,30 and 90). The application of Metformin does not alter blood glucose to the experimental animals alongside the control group (P>0.05 for the three measured values at 0,30 and 90 minutes). Differences have been observed in animals that have been treated continuously with palm oil and Metformin which was treated during the last 30 days of the study. They showed a decrease in blood glucose and data was obtained for the reduction of the insulin resistance during the GTT results.

CONCLUSION

The application of Metformin reduces the insulin resistance, which is developed during the continuous use of palm oil. *For the first time in the literature, the antagonistic metformin influence is reported in palm oil treatment.*

Research continued with the determination of insulin in the experimental animal blood. **Table 1** shows the results of insulin in the blood. The effect of palm oil with or without Metformin in the blood concentrations of insulin at the large male mice * <<0.001 compared with group with palm oil alone.

Table 1. The results of insulin in the blood

Group	Insulin in the bloodngr/ml
Control	2.4 + 0.18
Metformin	2.1+ 0.2
Palme oil	2.9 + 0.05 a
Palm oil + Metformin	2.0 + 0.09 *

Efforts continued with the research of the effect of palm oil with or without metformin to interferon-gamma, TNF-α and IL-6 of male mice.

Figure 3 shows the results of the determination of INF-γ on day 30 and 60 from experiments on experimental adult animals. The results show that palm oil reduces interferon gamma levels. Metformin antagonizes the suppressive effect of palm oil in the interferon gamma. Statistically significant is the difference between palm oil + metformin and palm oil only (p <0.001)
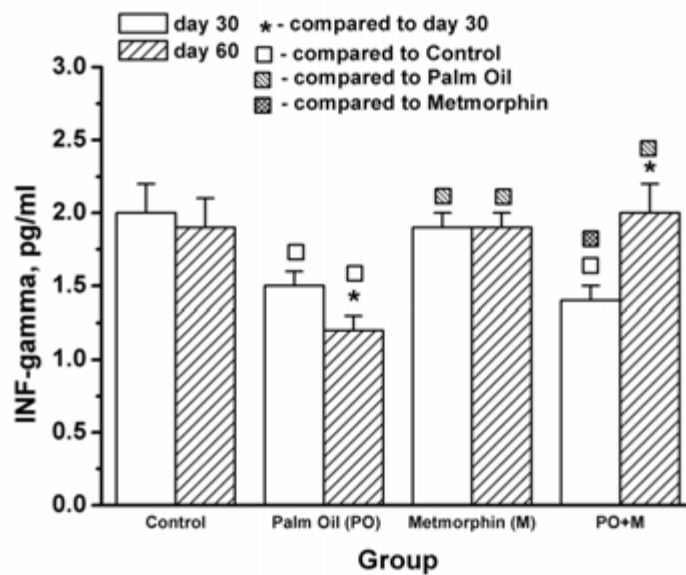
Figure 3. The levels ofINF-γin the blood of experimental mice continuously treated (30 and 60 days) with palm oil, metformin or combination with palm oil + metformin.

Statistical analysis:

One-Way ANOVA: P<0.0001, Bartlett: SD's belong to the same population, Bonferoni: critical T=3.308.

Conclusion: results of experimental animals from the interferon gamma research.

1. Treatment with palm oil is statistically significant leads to the decrease of (P <0.001 for both study periods) interferon gamma (INF-γ) unlike the control group.
2. Treatment with metformin alone does not change this indicator.
3. The combined treatment with palm oil and metformin has different effects for the period of 30 and 60 days: after 30 days of prolonged treatment, INF-γ had a typical level for the group receiving palm oil (P <0.001), whereas in the group treated continuously for 60 days, this level is approximately similar to the group that has received metformin (R <0.001).

Table 2. TNF-α (kg/ml) levels in the blood of the experimental adult animals treated continuously (30 and 60 days) with palm oil, metformin or in combination with palm oil + metformin. * P <0.001 in comparison with the control group, **a**-P <0.001, compared with the palm oil group only; **b**- <<0.001 compared with the 30-day research of the same group.

Group	TNF-α 30 days	TNF-α 60 days
Control	132.0 + 18.0	126.0 + 12.0
Metformin	116.0 + 9.0	111.0 + 14
Palme oil	184.0 + 11.0 *	198.0 + 8.0 *
Palme oil+metformin (30 last days)	179.0 + 7.2 *	121.0 + 11.8 a; b

Table 3. Levels IL-6 (kg / ml) in experimental animal blood treated continuously (30 and 60 days) with palm oil, metformin or in combination with palm oil + metformin.

Group	IL-6 30-days	IL-6 60-days
Control	980.0 + 22.6	1060.0 + 16.4
Metformin	1020.0 + 31.4	840. + 28.6
Palme oil	1280.0 + 48.4	1320.0 + 36.1
Palme oil + Metformin	1140.0 + 25.9	1012.0 + 46.0

Conclusions from TNF-α and IL-6 research:

1. Palm oil treatment increases the level of TNF-α and IL-6 on day 30 and on day 60 of the study.
2. Treatment with metformin alone does not change the two indicators.
3. Metformin decreases both TNF-α and IL-6 levels in mice blood, treated continuously with palm oil.

DISCUSSION

Metformin research has demonstrated that this pharmacological substance has the ability to antagonize the palm oil diabetogenic activity. During these experiments, something new is presented in the medical science: the continuous Palme oil application reduces the level of interferon gamma in the bloodstream, which corresponds to its diabetic activity. *An novelty for the effect of metformin is the interaction with the mechanisms through which palm oil reduces interferon gamma.* The results show that metformin antagonizes both the Palme oil's diabetogenic influence and its impact on interferon. The results from these studies give reason to suppose that palm oil causes prediabetes by reducing the interferon gamma, which is the important protector of immune cells and beta cells of the pancreas. (Durham *et al.* 2008; Frank *et al.* 2011; Tinworth *et al.,* 2010; Tinworth *et al.,* 2012; Wilcock *et al.*, 1994).

The results presented above, for the first time demonstrate that metformin antagonizes the effect of palm oil to 2 pro-inflammatory cytokines during scientific experiments. It is known that these cytokines grow in case of obesity. Metformin's ability to reduce its concentration is important for this pharmacological substance and drug applied in practice. Taken together, the results from carbohydrate metabolism research, interferon gamma and 2 pro-inflammatory cytokines give reason (base) to accept the effect of metformin on prophylaxisof pancreatic beta cells through the influence of immunological mechanisms. Future studies will show the importance of this assumption.

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