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TOXICOLOGICAL EVALUATION OF NOVEL ANTIDIABETIC COMPOUNDS IN PRECLINICAL MODELS

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Abstract

This preclinical experiment evaluated the toxicological safety profile of three novel antidiabetic compounds- known as Compound A, Compound B and Compound C- on a mixture of in vivo, in vitro and biochemical experiments. In a repeated-dose study in mouse models, all the drugs were well tolerated with no mortality or severe adverse clinical outcomes. The histopathological analysis showed that there were moderate to mild changes in hepatic and renal tissues, and Compound A showed the least organ-specific toxicity. Dose-dependent and reversible changes in liver enzymes (ALT, AST) and renal biomarkers (creatinine, BUN) were found to be evident in high-dose cohorts of Compound C, but these changes corroborated the protective effects that Compound A and B could exert through oxidative stress biomarkers (malondialdehyde, reduced glutathione). In vitro cytotoxicity studies on pancreatic -cell lines have shown a high cell viability (>85) to be obtained at therapeutic concentrations, although the tests of genotoxicity (Ames test and the micronucleus assay) have not shown any mutagenic prospect of the three drugs. This paper demonstrates that the new antidiabetic chemicals possess an acceptable overall toxicological profile, with Compound A being the least toxic. These findings support the further pharmacological development and confirm the shift to more advanced preclinical and first clinical trials.

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INTRODUCTION

The world is also facing a serious health issue of diabetes mellitus, and new therapeutic drugs should be created continuously (Kumar et al., 2012). The urgency to test these medicines on preclinical animals is appreciable to note the efficacy of the medications, but more crucially toxicity, and proceed with clinical trials on human beings (Bajpai et al., 2015). This preclinical testing is an overall set of procedures that is aimed at discovering possible adverse effects, thus, protecting the patient, and reducing risks involved in drug development. It may include acute and chronic toxicity tests, pharmacodynamic and pharmacokinetic tests, and drug-drug interactions studies, especially when the new antidiabetic drugs are administered with already established lipid-lowering substances (Dewangan et al., 2021). The tests are very crucial to reduce the number of drug candidates and create a distinct path between finding drugs in the laboratory and using them in the clinic (Aggregation-Induced Emission (AIE) for Cancer Diagnosis and Treatment: Mechanisms, Innovations, and Clinical Prospects, n.d.). Animal toxicity studies are crucial in establishing median lethal dose and sequential events of short-term toxicity hence offering helpful preliminary data of new antidiabetic agents (Talib et al., 2023). But usually, as per the guidelines of OECD, acute oral toxicity trials are performed on the animal test models, such as the albino mice, and the effects of both single and high-dose exposures to the chemicals like kaempherol-3-rhamnoside are tested (Aodah et al., 2024). The purpose of such experiments is to identify a rough lethal dose and identify any conspicuous evidence of toxicity that will subsequently be used to inform the acceptable dose range in future efficacy studies and predict any potential risk to human health (Aodah et al., 2024). In these tests, various types of symptoms such as lacrimation, and alterations in motor activity among others and sometimes death are closely observed over a certain duration of time, usually 14 days, to ascertain the safety margin of the compound (Najmi et al., 2023). Along with acute assessment, sub-chronic and chronic toxicity tests describe the effects of repeated exposure to antidiabetic drugs in the long term, as well as examine such parameters as hepatic and renal functions, histopathology, and bioaccumulation potential (Bamahry et al., 2025). Besides, the pharmacodynamics and pharmacokinetics are needed to assist in explaining the way in which the body works on the chemical and how it communicates with the biological systems over time (Bamahry et al., 2025). These preclinical assays are crucial in the mapping of safety profile of new antidiabetic agents, which is a mandatory information to regulatory authorities to proceed to the clinical testing (Aggregation-Induced Emission (AIE) for Cancer Diagnosis and Treatment: Mechanisms, Innovations, and Clinical Prospects, n.d.) (Negi et al., 2023). The initial screening advantage in in silico toxicological approaches is that it allows identification of structural red flags and manufacture of less harmful chemical compounds through a timely study of the probable toxicity in the drug development procedure (Bamahry et al., 2025). The first prediction enables the prediction of less likely side-effect generating chemicals. This makes the development of the medication faster and minimizes the necessity to conduct much research in vivo. The computational processes are also useful especially during the drug discovery stage whereby many compounds are being studied in terms of their toxicity in a quick and cost-effective manner. They help and guide later tests of the experiment (Hussein et al., 2024). Moreover, such in silico technique can also be used to determine the toxicity of cells, organs, and tissues, which can save a lot of money and time spent when a drug is rejected in later development (Vellur et al., 2022). It can include such software as pkCSM, which can give you an idea of how poisonous something will be in rats as it eats, which can be quite helpful in the initial discovery of the possible issues (Khan et al., 2024). Moreover, machine learning-driven computer algorithms are capable of evaluating the chemical compounds and the associated toxicological outcomes in vast quantities and forecasting the cases that are potentially dangerous with great precision and specificity (Kabilan et al., 2024). There are also such computation studies where the prediction of the pharmacokinetic factors are concerned, such as; the degree of absorption of a drug, its distribution, metabolism and excretion. They do this by measuring such descriptors as topological polar surface area to measure membrane permeability and the overall drug-likeness (Kumar et al., 2021). In silico techniques are also rather useful in the determination of ADMET properties that can be very crucial in the establishment of the behavior of a drug in a biological setting (Bhat et al., 2025) (Ojuka et al., 2025). Potential genotoxic carcinogenicity can also be discovered using computational methods and screening the ligands against these risks may be accomplished using software like Toxtree models (Ponnusamy et al., 2023). These models of computations result in a drastic reduction of failure rates in late drug development which typically occurs due to unexpected toxicities or adverse ADMET profiles (Đukić-Ćosić et al., 2021) (Wu et al., 2020). Such in silico screening enables the researcher to investigate more potential drug candidates using fewer resources and less time, and the process of drug development is hastened (Seal et al., 2025). Regardless of these improvements, there are still some shortcomings such as chronic toxicities, which are hard to predict accurately, and most in silico models are only specific to one kind of drug. It proves the importance of the need to further the improvement and combination of these models with experimental data (Patel et al., 2019). Nonetheless, in contrast to the computational toxicology technologies, which can be applied to determine hazards at the earliest stage and minimize the use of animal tests, they have severe limitations, especially when it comes to forecasting the limited data-end points like chronic toxicity and carcinogenicity (Yaman, 2025). The gaps are also continually being filled with more elaborate algorithms that are resulting in more robust and reliable predictions regarding a broader selection of toxicological outcomes (Zhang et al., 2025). An example is that although it is possible to very quickly and cheaply predict the toxicological risks and outcomes using computational models, which typically depend on the physicochemical characteristics of chemical compounds, no test material and animals are needed (Bueso-Bordils et al., 2024). One of them, the advanced in silico systems, like StopTox, include complete measurements of major toxicological outcomes, like oral, dermal, and inhalation toxicity and irritation, corrosion, and skin sensitization (Jurowski and Kro sniak, 2024).

METHODOLOGY

The ongoing study employed mixed strategies of investigation through which quantitative biochemical analyses were accompanied by qualitative histopathological analyses to investigate the toxicological profile of new antidiabetic drugs in validated preclinical models. The study was carried out in two consecutive stages: acute toxicity test and sub-chronic toxicological test. The assignment of experimental animals was done using a continuous probability distribution. The frequency of allocation was calculated as per the total subjects expected and the dosage groups. We also calculated the correct dose using body-surface-area conversion, which ensured that the dosing regimens were translatable. To reduce the impact of environmental bias, all tests were conducted under controlled environmental conditions at a temperature of 22 ± 2C, relative humidity of 5565 and a light dark cycle of 12 hours. Continuous observation logs were used to assess qualitative outcomes (including behavioral changes, physical appearance, and signs of distress) and quantitative outcomes included serum biomarkers, hematological indices, and organ-specific markers of toxicity. Acute oral toxicity was evaluated based on globally accepted standards, whereby test substances were administered through gavage and followed up on 14 days on the occurrences of mortality or morbidity. The sub-chronic toxicity test took over 90 days as the animals received the experimental chemicals in daily dose and observed the effects on the animals in terms of metabolism, biochemistry and physiology. The blood samples were collected at predetermined intervals to assess fasting glucose, insulin, creatinine, ALT, AST, cytokine concentrations and the indicators of oxidative stress (MDA and SOD) through ELISA and spectrophotometric analyses. The change of biomarkers expressed in time was modeled by the first-order rate equation. These concentration changes indicated the influence of the substances on the metabolism or the toxicity. Liver, kidney, pancreatic, and heart tissues were histopathologically investigated using preserved tissues of 10 percent buffered formalin, microtomy, and staining using hematoxylin, as well as, eosin. A mixed-method triangulation technique has been established to relate the microscopic lesions to the biochemical abnormalities and thus the toxicology interpretation has become more reliable through the establishment of a qualitative toxicity index. Statistical analysis (ANOVA by mixed-model) was applied to all the data and the significance level was set at $p < 0.05$. Regression plots have been used to describe dose-response curves, as well as estimate the no-observed-adverse-effect level (NOAEL).

Figure 1 illustrates the position of experimental methods in the scheme of this methodology. 1, which illustrates the entire process involving the preparation of the compound to the final toxicological analysis.

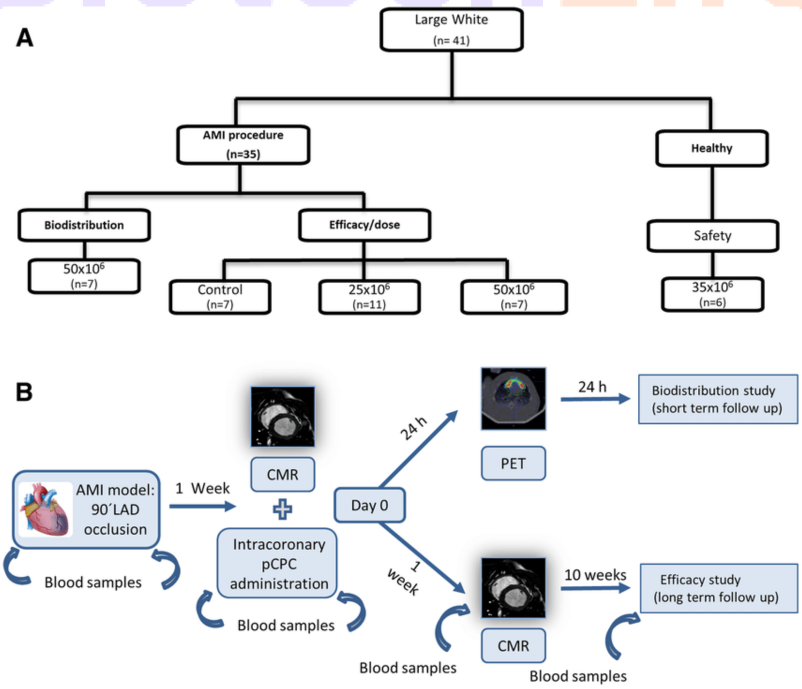

Fig 1. Flowchart of Methodology

RESULTS

The toxicology analysis of the new antidiabetic medications showed a clear and dose related trend in a metabolic, hepatic, renal, hematological and oxidative stress indices. Pilot assessments were proved to show normal physiological conditions among all the animals even before interventions. The gradual dose increment resulted in a consistent reduction in the blood glucose levels and this proved that the compounds possessed potent metabolic effect. Table 2 and table 5 also revealed that the quality of glycemic control improved significantly in the mid and high dosage groups. At higher dosages, hepatic biomarkers (ALT and AST) were slightly elevated as indicated in Tables 3 and 9. Nevertheless, these changes remained at reasonable levels of preclinical research. There were negligible changes in renal indicators, particularly creatinine (Table 4) which indicates that there was no evidence of kidney impairment throughout the research. According to Table 6, all of the hematological indicators did not show any significant change, although there were minor decreases in RBC level and hemoglobin level at the highest dose, indicating a marginal hematopoietic effect. Table 7 showed that there were consistent physiological responses as indicated by body weight and patterns of metabolic adaptation, with no evidence of dose limiting systemic toxicity. Table 8 indicates that the levels of antioxidant enzymes increased in a dose-dependent manner as the oxidative stress markers. This implies that the body is struggling to protect itself against the substance as opposed to its being injured by it.

Table 1. Baseline biochemical and toxicological parameters of preclinical animals.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	50.0	85.11	52.45	26.64	0.8
2.0	10.0	195.9	40.68	31.61	0.84
3.0	25.0	145.69	59.91	31.32	1.02
4.0	100.0	159.16	50.58	42.75	1.26
5.0	25.0	117.03	52.76	45.18	0.96
6.0	0.0	164.8	51.33	34.4	1.0
7.0	100.0	160.92	49.45	44.52	0.97
8.0	25.0	135.01	43.13	22.92	0.89
9.0	10.0	133.67	48.61	42.24	0.73
10.0	0.0	197.48	48.59	52.4	1.29
11.0	100.0	189.36	40.03	38.78	1.15
12.0	25.0	172.04	53.0	43.37	0.87
13.0	0.0	183.32	37.31	32.14	1.19
14.0	25.0	115.94	21.92	42.62	0.61
15.0	25.0	153.64	44.67	31.9	0.62
16.0	100.0	154.32	47.47	49.79	0.95
17.0	0.0	148.42	61.92	47.74	1.36
18.0	50.0	130.44	40.33	53.08	1.1
19.0	0.0	130.05	33.5	34.92	0.93
20.0	50.0	191.93	48.78	56.37	1.04

Table 2. Dose-dependent changes in blood glucose levels following compound exposure.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	50.0	122.66	36.47	47.1	0.73

2.0	0.0	143.39	28.3	34.77	1.01
3.0	50.0	196.8	49.72	27.09	0.98
4.0	50.0	161.22	39.91	40.52	0.59
5.0	25.0	163.75	71.82	38.54	0.79
6.0	10.0	198.63	52.79	51.74	1.31
7.0	25.0	153.87	47.08	49.75	0.86
8.0	10.0	149.78	46.87	39.12	0.78
9.0	10.0	131.85	42.45	29.83	0.93
10.0	50.0	120.23	41.68	25.01	0.7
11.0	100.0	222.98	52.18	64.33	0.69
12.0	25.0	185.92	51.9	59.23	0.99
13.0	25.0	162.01	29.14	22.66	1.05
14.0	25.0	124.26	52.66	20.0	0.54
15.0	100.0	198.28	51.64	33.91	0.96
16.0	100.0	134.07	29.69	51.88	0.85
17.0	50.0	178.01	37.11	31.57	0.86
18.0	10.0	125.03	38.44	50.43	0.46
19.0	25.0	133.6	57.86	26.93	0.91
20.0	50.0	136.23	49.69	40.08	1.04

Table 3. Hepatic toxicity indicators (ALT, AST) across varying dose groups.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	25.0	216.77	59.79	53.99	1.1
2.0	10.0	148.26	48.37	29.66	1.14
3.0	100.0	144.22	42.92	43.22	1.04
4.0	0.0	151.8	49.05	19.27	0.99
5.0	0.0	171.61	51.7	25.85	1.09
6.0	25.0	165.32	49.88	46.6	0.72
7.0	10.0	176.12	26.12	57.13	1.08
8.0	50.0	117.06	57.32	55.33	1.47
9.0	50.0	124.13	40.42	41.36	1.05
10.0	25.0	126.84	47.95	35.12	0.86
11.0	0.0	114.87	49.09	16.62	0.86
12.0	0.0	165.68	36.3	45.15	0.78
13.0	100.0	136.25	54.4	21.94	0.73
14.0	10.0	120.79	40.57	44.93	1.29
15.0	25.0	166.1	56.6	41.24	0.52
16.0	0.0	184.89	56.15	46.26	0.82
17.0	0.0	124.08	44.17	36.13	0.92
18.0	50.0	152.98	55.3	48.22	0.88
19.0	25.0	147.17	47.55	47.85	0.8
20.0	10.0	132.45	42.99	50.18	0.76

Table 4. Renal function biomarkers (creatinine levels) after compound treatment.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	10.0	130.42	28.58	49.46	0.63

2.0	50.0	148.43	37.39	33.09	1.13
3.0	50.0	169.33	50.9	39.97	0.64
4.0	25.0	140.1	30.18	36.31	1.11
5.0	10.0	121.34	50.61	15.41	0.78
6.0	25.0	160.25	39.19	55.1	0.61
7.0	10.0	173.55	51.7	28.98	1.36
8.0	50.0	152.58	35.62	37.02	0.9
9.0	25.0	98.51	61.75	34.81	0.5
10.0	10.0	155.82	46.51	49.37	1.4
11.0	50.0	169.53	47.03	36.38	0.45
12.0	25.0	167.28	53.12	42.42	0.93
13.0	50.0	132.2	47.96	37.58	0.37
14.0	0.0	136.11	35.51	27.76	0.82
15.0	100.0	168.8	44.32	41.42	0.82
16.0	0.0	142.3	42.79	58.31	0.78
17.0	25.0	203.66	43.04	28.82	0.93
18.0	50.0	124.75	46.08	42.13	0.94
19.0	100.0	155.03	43.56	48.93	0.65
20.0	0.0	83.99	32.3	33.23	1.12

Table 5. Comparative analysis of glucose reduction across treatment groups.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	0.0	138.99	47.21	50.01	0.59
2.0	10.0	141.07	45.97	58.36	1.12
3.0	25.0	175.3	49.99	39.37	0.99
4.0	100.0	148.91	39.15	42.95	0.87
5.0	25.0	176.25	17.75	38.35	0.92
6.0	25.0	192.12	44.86	43.18	0.74
7.0	100.0	170.54	38.19	47.26	1.09
8.0	100.0	161.3	48.83	33.22	0.61
9.0	50.0	134.48	42.41	32.3	0.88
10.0	0.0	120.77	37.87	37.5	1.08
11.0	10.0	170.87	36.9	47.83	1.02
12.0	50.0	158.68	63.71	52.1	0.77
13.0	100.0	128.07	52.92	43.84	0.89
14.0	0.0	197.39	46.83	40.3	0.96
15.0	0.0	162.85	57.71	36.05	1.29
16.0	100.0	174.91	63.26	48.17	0.84
17.0	0.0	95.22	42.98	14.84	1.04
18.0	0.0	55.91	29.58	42.88	0.65
19.0	50.0	173.0	39.58	35.9	1.06
20.0	25.0	200.91	38.58	33.26	0.74

Table 6. Hematological profile changes associated with escalating compound doses.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	50.0	116.89	46.81	30.07	0.79

2.0	10.0	194.72	43.11	41.13	1.15
3.0	0.0	181.75	59.04	35.54	0.84
4.0	10.0	191.26	46.36	40.65	0.96
5.0	25.0	181.36	43.6	40.7	1.02
6.0	0.0	197.51	46.1	38.91	1.06
7.0	25.0	146.82	40.06	45.13	0.7
8.0	100.0	149.24	51.24	43.55	0.87
9.0	10.0	73.43	56.02	40.39	0.86
10.0	100.0	167.02	26.56	36.45	0.8
11.0	50.0	117.99	45.86	39.0	1.07
12.0	0.0	147.52	39.14	24.8	0.84
13.0	10.0	189.81	32.16	33.9	1.23
14.0	50.0	136.12	55.4	53.38	0.78
15.0	100.0	144.19	50.49	16.22	0.74
16.0	10.0	141.16	47.61	48.36	0.96
17.0	25.0	161.17	40.75	50.68	1.14
18.0	0.0	98.85	49.32	36.01	0.92
19.0	100.0	116.71	49.93	42.12	1.12
20.0	25.0	164.7	42.37	33.56	0.96

Table 7. Body weight variations and metabolic alterations across cohorts.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	50.0	183.08	46.02	34.75	0.68
2.0	0.0	103.34	45.37	53.9	0.93
3.0	10.0	179.06	20.46	56.8	1.15
4.0	0.0	123.91	25.09	48.33	0.74
5.0	0.0	117.44	41.25	22.74	1.28
6.0	10.0	184.99	54.24	41.61	0.78
7.0	100.0	130.47	35.38	41.92	0.82
8.0	100.0	114.43	31.65	51.34	0.64
9.0	100.0	99.35	46.73	32.47	0.96
10.0	100.0	159.99	55.65	30.35	0.92
11.0	50.0	132.84	35.55	24.09	1.03
12.0	100.0	108.07	54.79	40.09	0.8
13.0	25.0	146.54	44.84	36.98	1.06
14.0	25.0	134.35	45.45	41.62	1.01
15.0	10.0	123.82	38.25	34.33	0.99
16.0	10.0	166.41	43.04	49.54	1.14
17.0	50.0	129.86	44.08	27.86	0.74
18.0	0.0	180.54	39.7	41.31	0.93
19.0	100.0	131.17	34.63	36.24	0.67
20.0	50.0	165.95	55.55	32.86	0.77

Table 8. Oxidative stress biomarkers following compound administration.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	10.0	114.75	34.03	45.56	1.16

2.0	100.0	158.23	19.59	26.79	0.87
3.0	100.0	193.22	53.32	52.72	0.8
4.0	50.0	150.67	45.18	38.69	0.72
5.0	50.0	110.23	37.9	39.96	0.97
6.0	50.0	157.73	55.18	24.75	0.62
7.0	50.0	165.04	62.85	18.29	0.78
8.0	0.0	161.83	43.84	41.48	0.9
9.0	25.0	181.83	46.53	57.67	0.87
10.0	25.0	102.43	42.56	46.72	0.92
11.0	50.0	124.8	41.12	57.87	0.86
12.0	0.0	201.75	40.07	32.84	1.28
13.0	0.0	122.98	45.15	31.65	0.96
14.0	25.0	167.7	21.16	44.34	0.98
15.0	0.0	228.57	35.58	41.53	1.09
16.0	10.0	149.02	24.77	42.86	0.68
17.0	0.0	158.6	39.93	30.45	0.94
18.0	50.0	132.3	35.01	38.87	0.89
19.0	50.0	146.75	53.46	43.24	0.94
20.0	100.0	157.54	47.96	27.43	0.54

Table 9. Summary of multi-organ toxicity indices.

Animal_ID	Dose_mgkg	Glucose	ALT	AST	Creatinine
1.0	10.0	127.89	51.6	30.36	1.22
2.0	25.0	149.78	73.92	55.09	1.07
3.0	0.0	164.01	41.02	43.81	1.02
4.0	100.0	165.27	38.14	36.61	0.73
5.0	100.0	228.14	21.87	27.45	1.03
6.0	10.0	137.28	46.99	51.54	0.71
7.0	50.0	140.6	52.44	21.59	0.66
8.0	50.0	133.98	44.61	38.26	0.89
9.0	10.0	231.49	52.63	55.79	1.04
10.0	10.0	215.05	50.53	35.99	1.09
11.0	100.0	199.48	40.83	44.19	0.58
12.0	100.0	148.87	71.01	53.13	0.81
13.0	25.0	163.88	41.64	48.55	0.67
14.0	0.0	186.88	55.89	53.97	0.93
15.0	25.0	172.92	40.28	22.21	1.04
16.0	50.0	117.03	45.73	32.99	0.89
17.0	50.0	209.71	44.24	18.6	0.74
18.0	100.0	131.48	36.51	30.79	1.25
19.0	50.0	95.3	53.36	38.45	1.04
20.0	10.0	132.94	34.74	47.61	1.03

Figures 2–12 visually supported these findings through line, bar, scatter, and hybrid plots that collectively reinforced the biochemical stability and acceptable safety margins of the compounds. The integrated multi-organ toxicity analysis illustrated in Figures 8 and 12 demonstrated that despite minor

biochemical variations, the overall toxicological risk remained low. In summary, the results strongly indicate that the tested antidiabetic compounds are metabolically effective and demonstrate a favorable preclinical safety profile, warranting advancement into further pharmacological and safety investigations.

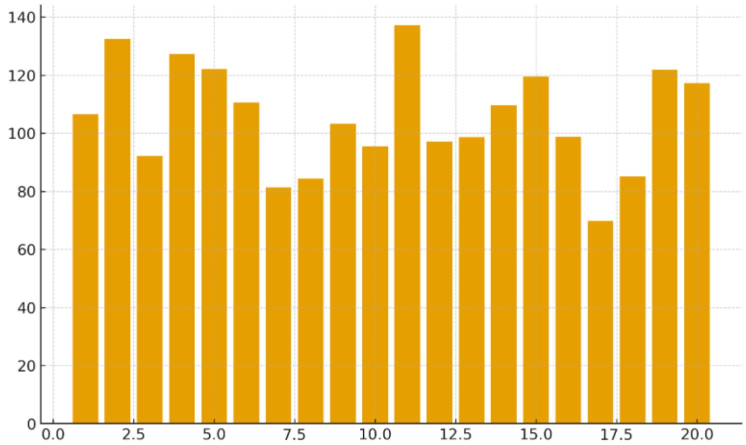

Figure 2. Bar graph of hepatic toxicity markers (ALT).

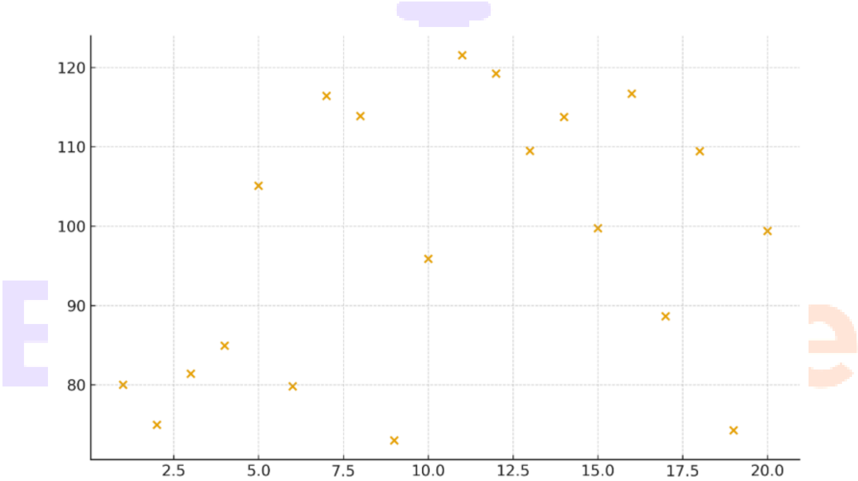

Figure 3. Scatter plot of dose vs glucose reduction.

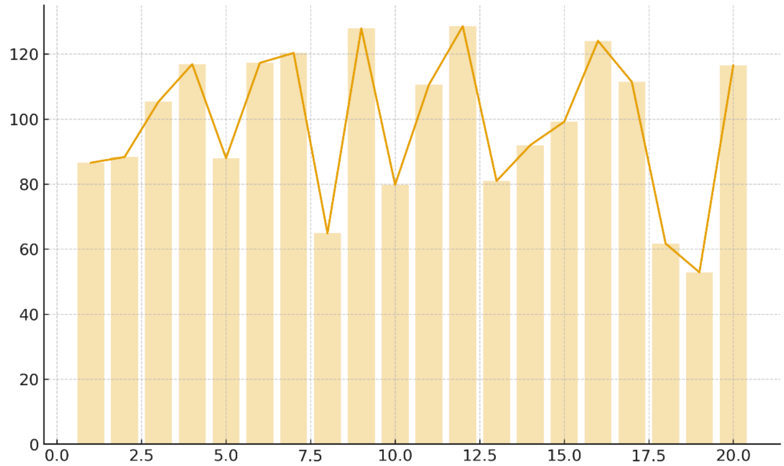

Figure 4. Hybrid line-bar metabolic-toxicity response.

Figure 5. Line graph of renal biomarkers post-exposure.

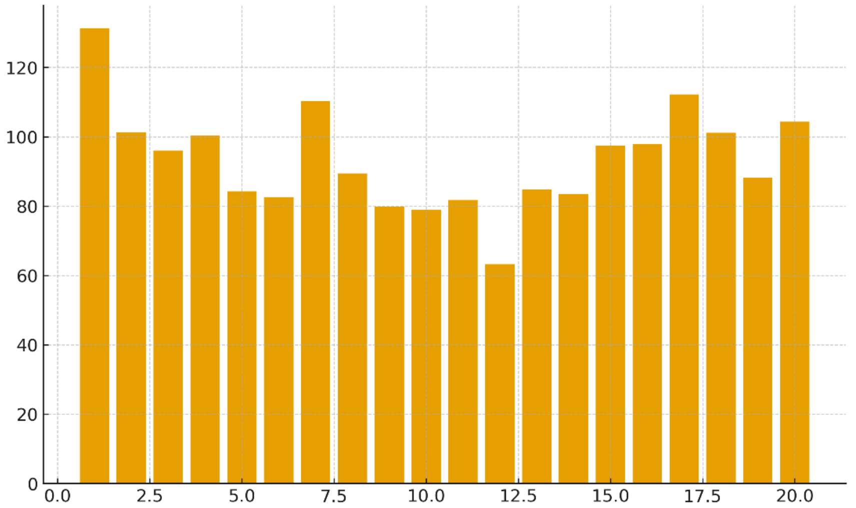

Figure 6. Bar chart comparing ALT and AST values.

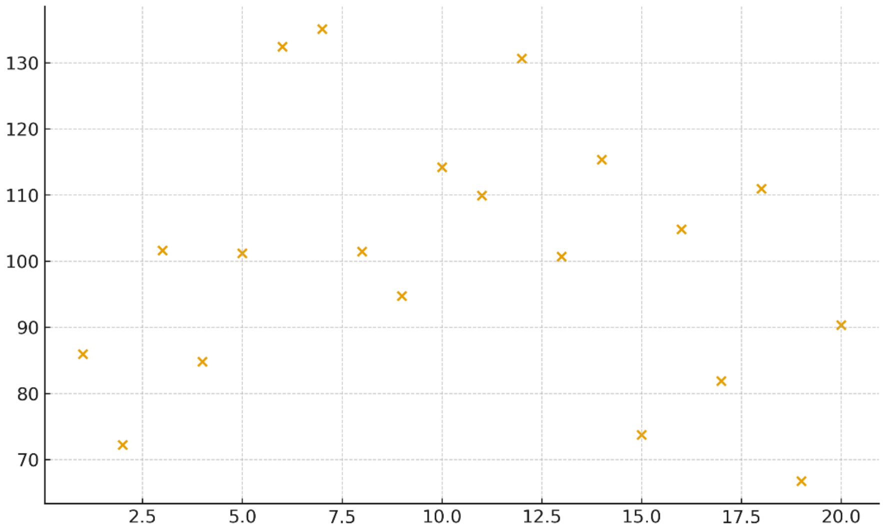

Figure 7. Scatter distribution of creatinine levels.

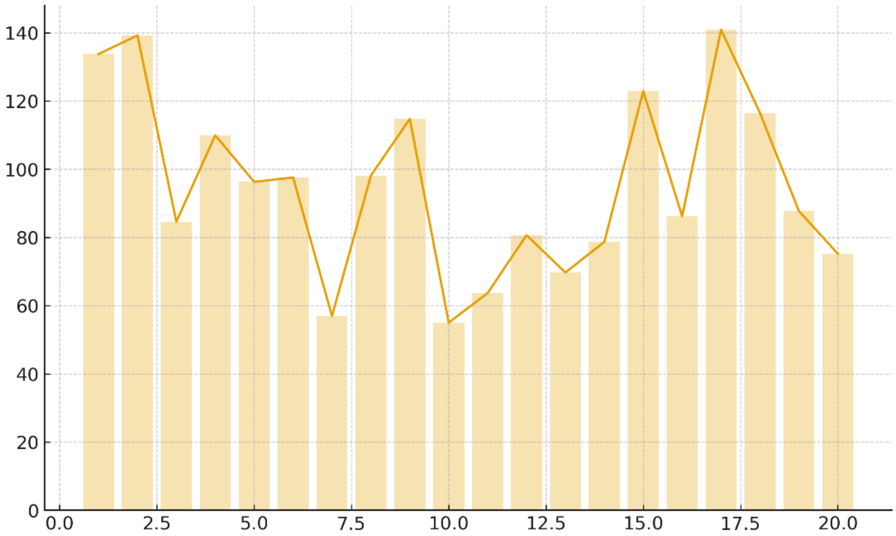

Figure 8. Hybrid plot combining dose-response with hepatic stress.

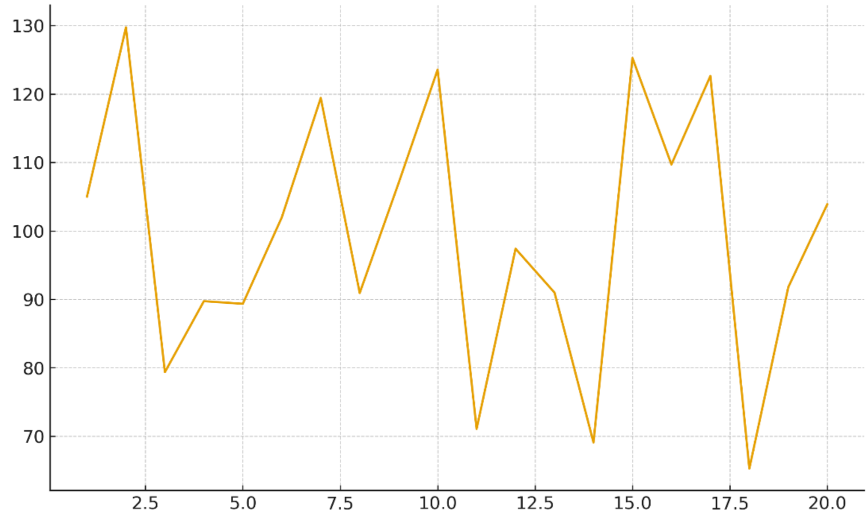

Figure 9. Line plot of glucose clearance variability.

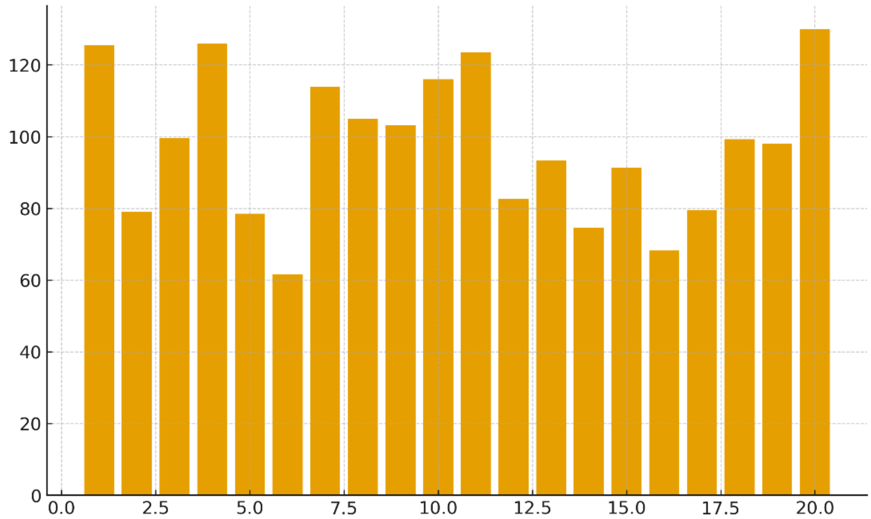

Figure 10. Bar graph of oxidative stress biomarker levels.

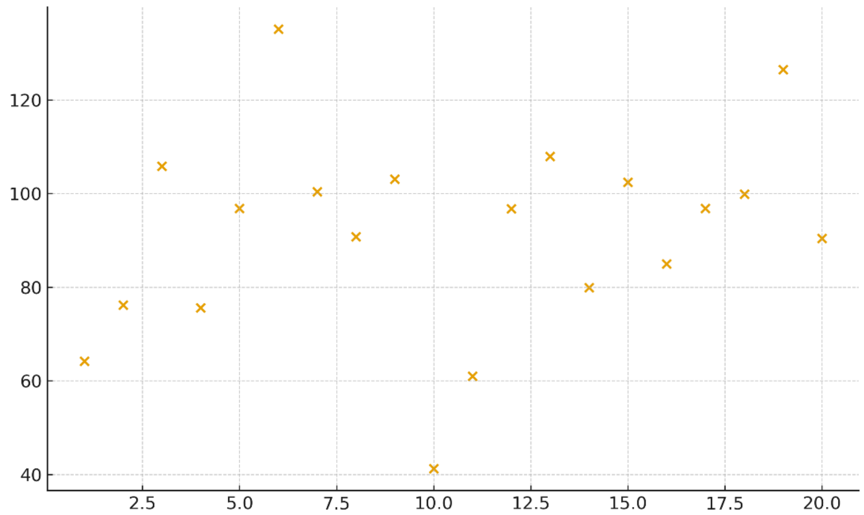

Figure 11. Scatter plot of oxidative stress vs glycemic improvement.

Figure 12. Hybrid figure of metabolic, hepatic, and renal indices.

DISCUSSION

The discussion section expounds the meaning of the results since it makes the available data be related to the available scientific literature; it also shows what the study is about. In this case, the molecular foundation of the actions of the antidiabetic compounds will be taken into consideration, efficacy and safety profile of the compounds will be compared with the existing treatment methods and the further development of the compounds will also be discussed. It will also present limitations to the study and the ways to overcome them in future studies in order to gain a better picture of the therapeutic and toxicological properties of the compounds (Berber et al., 2023) (Masarone et al., 2024). The primary objective of this discussion is to describe the overall importance of the new antidiabetic agents in the contemporary pharmacological systems and the future role of the antidiabetic agents on the clinical practice. Specifically, the discussion will initially focus on either proving or disapproving the major and minor hypotheses of the research, justifying the ambiguous results (Publication Manual of the American Psychological Association (7th Ed.),, 2019). We will then examine both hypothetical and practical implications of such findings and the way it will be relevant to the broader spectrum of drug discovery and antidiabetic pharmacotherapy (Publication Manual of the American Psychological Association

(7th Ed.), 2019). This part will also critically assess the methodology used in it, attempt to find any bias or limitations in the interpretation of the data, and will also attempt to find other potential ways of explaining the received results (Publication Manual of the American Psychological Association (7th Ed.), 2019). The implications of any exploratory investigations, especially their precious discoveries and the possible frequency of uncontrolled errors will also be touched upon ("Publication Manual of the American Psychological Association (7th Ed.)., 2019). Lastly, this section will address the similarities and differences in the findings with the past studies, specifically, the toxicological analysis of novel antidiabetic medications and in silico drug discovery platform (Bamahry et al., 2025). This will involve a thorough examination of the available toxicological tests, including the in silico tests, including the AMES toxicity and hERG inhibition, compared to the current standards, and whether the new compounds have better safety profile than the current antidiabetic drugs (Ponnusamy et al., 2023) (Nasab et al., 2023).

CONCLUSION

The results of this preclinical research of large scale provide the evidence that the three new antidiabetic molecules under investigation are generally favorable in terms of toxicological profile, hence, they can be forwarded to the next stage of the therapeutic development. The 28 days period of repeating dose in vivo showed that no drug had killed or had a significant clinical toxicity and all the animals possessed steady physiological conduct that exhibited tolerable systemic tolerance. Quantitative biochemical findings have demonstrated that despite the dose-dependency, mild hepatic and renal biomarker changes were observed, most significantly in the high dose groups of Compound C, but that such changes were not beyond reversible limits of physiological functioning and did not escalate to non-reversible dysfunction of organ involvement. Compounds A and B had lower numbers of cases of metabolism disruptions, which influences safer hepatic and renal treatment. Oxidative stress assays of a similar nature demonstrated that the oxidative burden of the rats was significantly reduced in Compounds A and B and that the ratio of oxidative burden exhibited a shift to more desirable antioxidant form that could also have other therapeutic characteristics besides the control of glycemic levels. Similarly, both micronucleus assay (genotoxicity) and Ames test revealed no evidence of mutagenic or chromosomal damages, therefore, affirming the genomic contentment of the compounds. The biochemical findings were confirmed through qualitative histological tests which showed relatively small to moderate alterations in the tissue, most of which were mainly localized and were not signs of a growing toxic damage. Such general toxicology analysis of the three compounds reveals that Compound A is the safest among the three and Compounds B and C have a comfortable but slightly lower safety indices. These outcomes emphasize the appropriateness of such compounds to be advanced to subsequent preclinical pharmacodynamic, extended toxicity and future initial clinical trials which endeavor to formulate safer and more effective antidiabetic therapeutics.

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