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Title: Dual magnetic field therapy mitigates LPS-induced pancreatic injury by preserving islet structure and endocrine function in rats.

Short title: Magnetic field therapy against LPS-induced pancreatic damage.

Abstract

Purpose: Sepsis is a life-threatening systemic inflammatory response that can lead to multiorgan failure, including pancreatic dysfunction. This study aimed to investigate the potential protective effects of radiofrequency (RF) and pulsed magnetic field (PM) therapies against lipopolysaccharide (LPS)-induced pancreatic injury in rats.

Materials and methods: Forty female Wistar albino rats were randomly assigned to five groups (n=8 per group): Control, LPS, LPS + RF, LPS + PM, and LPS + PM + RF. LPS was administered intraperitoneally (5 mg/kg), followed by RF (30 minutes) and/or PM (3 hours) exposure. Pancreatic tissues were examined histopathologically and immunohistochemically for insulin, glucagon, and amylin expression.

Results: LPS administration resulted in significant histopathological damage, including hyperemia, edema, and inflammatory infiltration, as well as reduced insulin and amylin immunopositivity and increased glucagon expression in islets. Both RF and PM treatments alleviated these changes, with the combined PM+RF application showing the most prominent protective effects, restoring normal histological architecture and hormonal profiles.

Discussion: RF and PM therapies, particularly in combination, exhibit significant protective effects against sepsis-induced pancreatic injury by mitigating inflammation and preserving islet cell function. These findings highlight a novel non-pharmacological approach for supporting pancreatic health in inflammatory conditions.

Keywords: Sepsis, pancreas, radiofrequency, pulsed magnetic field, LPS.

Makale başlığı: Dual manyetik alan tedavisi, sıçanlarda LPS ile indüklenen pankreas hasarını, adacık yapısını ve endokrin fonksiyonu koruyarak azaltır.

Kısa başlık: LPS kaynaklı pankreas hasarına karşı manyetik alan tedavisi.

Öz

Amaç: Sepsis, pankreas disfonksiyonu da dahil olmak üzere çoklu organ yetmezliğine yol açabilen, yaşamı tehdit eden sistemik bir inflamatuar yanıttır. Bu çalışmanın amacı, lipopolisakkarit (LPS) ile indüklenen pankreas hasarı üzerinde radyo frekans (RF) ve darbeli manyetik alan (PM) tedavilerinin koruyucu etkilerini değerlendirmektir.

Gereç ve yöntem: Kırk dişi Wistar albino rat Kontrol, LPS, LPS+RF, LPS+PM ve LPS+PM+RF olmak üzere rastgele beş gruba ayrıldı (n=8). LPS, intraperitoneal olarak (5 mg/kg) uygulandı, ardından RF (30 dakika) ve/veya PM (3 saat) uygulamaları yapıldı. Pankreas dokuları histopatolojik olarak incelendi ve immünohistokimyasal olarak insülin, glukagon ve amilin ekspresyonları değerlendirildi.

Bulgular: LPS uygulaması sonucunda pankreaslarda hiperemi, ödem ve inflamatuar infiltrasyon gibi belirgin histopatolojik hasarlar gözlendi. Ayrıca adacık hücrelerinde insülin ve amilin ekspresyonları azaldığı, glukagon ekspresyonu ise arttığı dikkati çekti. Hem RF hem de PM tedavilerinin bu değişiklikleri hafifletti saptandı. Özellikle PM+RF kombinasyonu, normal histolojik yapının ve hormonal expresyonların en belirgin şekilde düzeltilmesini sağladı.

Sonuç: RF ve PM tedavileri, özellikle birlikte uygulandıklarında, sepsise bağlı pankreas hasarına karşı önemli koruyucu etkiler göstermektedir. Bu etkiler, inflamasyonu azaltma ve adacık hücre fonksiyonlarını koruma yoluyla gerçekleşmektedir. Bulgular, inflamatuar durumlarda pankreas sağlığını desteklemek için farmakolojik olmayan yeni bir yaklaşımı ortaya koymaktadır.

Anahtar kelimeler: Sepsis, Pankreas, Radyo Frekans, Darbeli Manyetik Alan, LPS.

Introduction

Sepsis remains a leading cause of mortality in critical care settings, frequently resulting in multiorgan dysfunction due to dysregulated inflammatory responses [1]. Among the affected organs, especially its endocrine component of the pancreas, is particularly vulnerable to systemic inflammatory injury [2]. Lipopolysaccharide (LPS), a major component of the outer membrane of Gram-negative bacteria, is widely used to simulate the pathophysiological features of sepsis in experimental models [3]. LPS initiates a potent immune response through Toll-like receptor 4 signaling, triggering the release of pro-inflammatory cytokines such as interleukin (IL)-1 beta and tumor necrosis factor-alpha (TNF-α), and which contribute to tissue damage and endocrine dysregulation [4].

The islets of Langerhans, composed of insulin and amylin producing β-cells, glucagon-secreting α-cells are critical regulators of glucose homeostasis [5]. Inflammatory injury to these cell populations during sepsis can lead to impaired glycemic control and metabolic instability [6]. Studies have shown that LPS exposure leads to a reduction in insulin and amylin expression, accompanied by an increase in glucagon levels, thus promoting hyperglycemia and energy imbalance [7, 8].

Recent advances in physical medicine have introduced non-invasive modalities such as radiofrequency (RF) electromagnetic fields and pulsed magnetic fields (PM) as promising therapeutic tools for modulating inflammation and promoting tissue repair [9]. RF has been shown to influence cellular activity through non-thermal mechanisms, including modulation of ion channels, enhancement of calcium flux, and alteration of gene expression [10]. Likewise, PM therapy has been demonstrated decrease oxidative stress, suppress nuclear factor kappa β (NF-κβ) activation, and support mitochondrial homeostasis, making it a potential anti-inflammatory strategy in acute and chronic injury models [11, 12].

Although both RF and PM therapies have demonstrated therapeutic benefits in other tissue types, their combined use in the context of LPS-induced pancreatic injury has not been systematically evaluated. Hence, this study aimed to investigate the protective effects of RF and PM, individually and in combination, on pancreatic damage induced by LPS in rats (Figure 1). Histopathological and immunohistochemical assessments of insulin, glucagon, and amylin were conducted to elucidate the effects of these biophysical interventions on islet structure and function.

Material and method

Animals and ethical approval

In this study, pancreatic tissues from rats used in a previous investigation that examined the effects of RF and PM on kidney tissue were evaluated; no new animal experiment was conducted [13]. During the original study, while the effects of RF and PM on other tissues were also being assessed, notable improvements were observed in the pancreatic tissues, prompting a decision to further evaluate them. Accordingly, approval was obtained from the Local Ethics Committee for Animal Research at Süleyman Demirel University for the publication of findings derived from the pancreatic tissues (approval no: SDU HADYEK 556, and dated 12.06.2025). All experimental procedures in the original kidney-focused study were conducted in accordance with the Animal Research: Reporting of In Vivo Experiments (ARRIVE) 2.0 guidelines. This study was also supported by the Scientific Research Projects Coordination Unit of Süleyman Demirel University (project code: TSG-2024-9515).

Forty adult, female Wistar albino rats (weighing 300-350 g) were housed under standard laboratory conditions, including a controlled temperature of 21-22°C, relative humidity of 60±5%, and a 12-hour light/dark cycle. All animals had free access to a standard chow diet (Korkuteli Yem, Antalya, Türkiye) and water ad libitum.

Experimental design

In this study, forty adult female Wistar Albino rats, 10-12 weeks old, weighing 250-350 g, obtained from Süleyman Demirel University, Faculty of Medicine, Animal Experiments Laboratory were used. The rats were kept at 22-24ºC, 12 hours in the light and 12 hours in the dark. Ad libitum feeding regime was applied. Euro type-4 cages were used for rats.

Forty rats were divided into 5 groups of 8 rats each. Groups;

Control: After a single dose of intraperitoneally (ip) saline injection, it was left in the non-activated unit for 6 hours.

LPS: Single dose of ip 5 mg/kg LPS was administered and left in the non-activated unit for 6 hours.

LPS+RF: Single dose of ip 5 mg/kg LPS followed by RF activated for 30 minutes and then left in the inactivated unit until the 6th hour.

LPS+PM: Following a single dose of ip 5 mg/kg LPS administration, PM was activated for 3 hours and then left in the inactivated unit until the 6th hour.

LPS+PM+RF: Single dose of ip 5 mg/kg LPS followed by activated PM (for 3 hours) and RF (for 30 minutes) combined application and left in the inactivated unit until the 6th hour**.**

In a preliminary phase of the same experiment, the timing of the applications was determined to be optimal. All rats were euthanized six hours after LPS injection under anesthesia with ketamine (90 mg/kg) and xylazine (10 mg/kg). Euthanasia was conducted through surgical exsanguination, with blood samples obtained via puncture of the inferior vena cava following a midline abdominal incision. Pancreatic tissues were promptly harvested from each subject and fixed in 10% neutral buffered formalin for subsequent histopathological examination utilizing hematoxylin and eosin (HE) staining, alongside immunohistochemical assessment of insulin, glucagon, and amylin expression.

Histopathological analysis

Pancreatic tissues were excised and immediately preserved in 10% buffered formalin within ten minutes post-mortem. The samples were fixed for 48 hours prior to standard tissue processing using a fully automated tissue processor (Leica ASP300S, Leica Microsystems, Nussloch, Germany). Following fixation, the tissues were embedded in paraffin wax, and 5 µm-thick sections were obtained using a fully automated rotary microtome (Leica RM2155, Leica Microsystems, Nussloch, Germany). The sections were then dried, deparaffinized, and rehydrated through a graded series of alcohols. Hematoxylin and eosin staining method was performed, with Harris hematoxylin applied for five minutes and eosin for two minutes (Tek-Path, Izmir, Türkiye). After staining, the slides were mounted with coverslips and examined under a light microscope (Zeiss Axioscope 5 trinocular microscope, Carl Zeiss Microscopy GmbH, Jena, Germany). The entire histological procedure—from fixation to staining—was completed within one week to ensure optimal tissue preservation.

Microscopic changes were evaluated in a blinded manner. Histopathological evaluation of the pancreatic tissue was performed in ten distinct regions per rat. Hyperemia, edema, and inflammation were individually scored on a semi-quantitative scale ranging from 0 to 3, with 0 indicating no pathological alteration and 3 representing severe changes. Degeneration was scored based on the number of damaged cells observed in each section (Table 1). Each pancreatic sample was independently analyzed twice by the same experienced pathologist. Additionally, 100 Langerhans islets were randomly selected from each sample, and cell counting was performed using ImageJ software (National Institutes of Health, Bethesda, MD, USA). The software's counter tool allowed cells to be marked with colored dots upon clicking. The final histopathological score for each animal was calculated as the average of the two independent assessments.

Immunohistochemical examination

Four serial sections were obtained from the previously prepared paraffin blocks and mounted on poly-L-lysine-coated slides. Immunohistochemical staining was performed using the streptavidin–biotin method, following the manufacturer's instructions, to detect the expression of glucagon (rabbit monoclonal anti-glucagon antibody [EP3070]; ab92517), insulin (rabbit monoclonal recombinant anti-insulin antibody [EPR17359], BSA- and azide-free; ab202760), and amylin (rabbit monoclonal anti-amylin/DAP antibody [EPR2255(138)]; ab254259) (Abcam, Cambridge, UK). The primary antibodies were diluted 1:100 in antibody dilution buffer (Thermo Fisher Scientific, MA, USA) and incubated with the tissue sections for 60 minutes. This was followed by incubation with a biotinylated secondary antibody and a streptavidin–alkaline phosphatase conjugate.

The secondary antibody was provided by a rabbit-specific HRP/DAB IHC Detection Kit—micro-polymer (ab236469, Abcam, Cambridge, UK), and diaminobenzidine (DAB) (DAB Substrate Kit, ab64238) was used as the chromogen. Tissue sections were incubated with DAB for 3 to 5 minutes. For negative controls, the antibody dilution solution was applied instead of the primary antibody. All immunohistochemical analyses were performed in a blinded manner by an experienced pathologist from an independent institution, who was unaware of the group assignments for each pancreatic tissue sample. Each antibody was evaluated separately. The percentage of positively stained cells was determined for each slide, and the average percentage of positive cells was calculated across all samples. Additionally, the number of positively stained cells per high-power field and the number of marker-positive cells per islet were counted and compared to those in the control group.

All nuclei within each Langerhans islet were counted, and the average number of nuclei per islet was calculated. For each sample, a minimum of five high-power fields (×40 magnification) were analyzed. Immunohistochemical evaluations were performed using ImageJ software (National Institutes of Health, Bethesda, MD, USA), and the resulting data were subjected to statistical analysis. Microphotographic documentation was conducted using the CellSens Life Science Imaging Software System (Olympus Corporation, Tokyo, Japan).

Statistical analysis

Prior to the study, a power analysis was conducted using G*Power software (version 3.1.9.7) to determine the minimum required sample size. Based on the parameters of effect size =0.8, α=0.08, and desired power (1-β)=0.95, a sample size of seven rats per group was determined to be sufficient.

Data were presented as medians, means ± standard deviations, frequencies, percentages, or minimum-to-maximum values, as appropriate. The normality and homogeneity of variance for continuous variables were assessed using the Shapiro-Wilk, Levene, and Kolmogorov-Smirnov tests. Variables following a normal distribution were expressed as mean ± standard deviation, while those not normally distributed were expressed as median and range.

For comparisons involving non-normally distributed data, the Kruskal-Wallis test followed by pairwise Mann-Whitney U tests were utilized. When data conformed to normality assumptions, one-way analysis of variance (ANOVA) with Tukey's post hoc test was applied. Immunohistochemical analysis involved quantification of the percentage of immunopositive cells. To evaluate the interactive effects of device treatments (RF and PM) and LPS exposure, two-way ANOVA was performed. All statistical analyses were conducted using GraphPad Prism version 10 (GraphPad Software, CA, USA), with significance set at $p<0.05$.

Results

Histopathological findings in pancreatic tissues

No significant gross pancreatic lesions were observed in any experimental group. However, histopathological analysis revealed marked degenerative and necrotic changes in the β-cells of the islets of Langerhans in both LPS-treated groups, accompanied by hyperemia, edema, and infiltration of inflammatory cells. These pathological alterations were notably attenuated in the RF, PM, and PM+RF treatment groups, with the PM+RF group demonstrating the most pronounced improvement compared to RF or PM administration alone (Figure 2).

Immunohistochemical evaluation of pancreatic tissues

In control animals, insulin- and amylin-immunoreactive β-cells were predominantly located in the central region of the islets of Langerhans, whereas glucagon-immunopositive α-cells were restricted to the periphery, reflecting normal islet cytoarchitecture. In stark contrast, the LPS group displayed a pronounced depletion of insulin- and amylin-positive β-cells, accompanied by a significant increase in glucagon-immunoreactive α-cells. Interestingly, amylin-immunoreactive cells were distributed across both central and peripheral regions of the islets in all groups.

Quantitative immunohistochemical analysis revealed a significant reduction in both the number and staining intensity of amylin-positive cells in the LPS group compared to controls. Similarly, insulin expression was markedly suppressed, while glucagon levels

were elevated, indicating severe disruption of islet cell function and hormonal regulation (Figure 3-5 and Table 2).

Therapeutic intervention partially mitigated these alterations. Among the treatment groups, the combination of PM and RF conferred the most pronounced protective effect, restoring islet architecture and hormonal marker expression closer to baseline levels.

This study demonstrated that LPS-induced pancreatic injury is characterized by significant histopathological damage and disruption of islet cell hormonal balance, including reduced insulin and amylin expression and increased glucagon levels. Treatment with RF and PM, particularly in combination, significantly mitigated these pathological changes and restored islet architecture and function. These findings suggest that the PM+RF combination offers a promising protective strategy against pancreatic damage associated with inflammatory stress.

Discussion

The findings of this study provide novel evidence that single or combined RF and PM therapies exert significant protective effects on pancreatic tissues subjected to LPS-induced sepsis. The observed histopathological and immunohistochemical changes indicate that these biophysical modalities can mitigate inflammatory injury and preserve endocrine homeostasis within the islets of Langerhans. The deleterious effects of LPS, including hyperemia, edema, inflammatory infiltration, and islet cell degeneration were markedly attenuated in the treatment groups, particularly when RF and PM were applied in combination.

The histopathological features in the LPS group align with previous reports highlighting the susceptibility of β-cells to inflammatory insults [14, 15]. These cells, with high metabolic activity and low antioxidant capacity, are highly vulnerable to oxidative and nitrosative stress triggered by sepsis [16-18]. The dramatic reduction in insulin- and amylin-expressing cells, along with an increase in glucagon-immunoreactive α-cells, supports the hypothesis that sepsis promotes selective β-cell dysfunction and α-cell hyperactivity, contributing to metabolic disarray.

The application of RF alone yielded modest improvements in islet morphology and hormone expression. This aligns with findings that RF energy, when delivered at controlled frequencies, may enhance cellular repair mechanisms without inducing thermal damage [19]. Mechanistically, previous studies have shown that RF exposure can activate transient receptor potential channels, modulate calcium influx, and suppress pro-inflammatory mediators such as IL-6 and TNF-α, thereby attenuating inflammation

[20-23]. In the present study, RF partially restored insulin and amylin levels, suggesting its role in promoting β-cell survival and function under inflammatory stress.

More pronounced effects were observed with PM treatment, which significantly improved both the structural integrity of the islets and the expression of endocrine hormones. PM is known to exert anti-inflammatory effects by downregulating NF-κβ activation and reducing the generation of reactive oxygen species [24]. The reduction in glucagon-positive α-cells in the PM group also suggests a rebalancing of hormonal output, potentially through modulation of intra-islet paracrine signaling and improved cellular viability.

The combined application of RF and PM produced the most robust therapeutic effect, with nearly complete restoration of normal islet architecture and hormonal profiles. The synergistic interaction between RF and PM may arise from their complementary mechanisms: RF modulates signal transduction and gene expression, while PM enhances antioxidant defense systems and mitochondrial function [10, 25]. Together, they likely reinforce cellular repair pathways, reduce apoptotic signaling, and enhance endocrine hormone secretion.

Interestingly, the beneficial effects of combination therapy were observed without the use of pharmacological agents, suggesting that biophysical interventions alone may be sufficient to counteract sepsis-induced pancreatic damage. This non-invasive approach offers an advantage in terms of safety, repeatability, and clinical applicability, particularly for critically ill patients where drug-induced hepatotoxicity or nephrotoxicity may pose additional risks.

The immunohistochemical analyses corroborated the histological findings, showing significant restoration of insulin and amylin expression and normalization of glucagon levels in the RF+PM group. These data suggest not only structural but also functional recovery of islet cells, which is essential for maintaining glucose homeostasis during systemic inflammation [26, 27]. Restoration of endocrine function may help reduce sepsis-related metabolic complications such as hyperglycemia, which is associated with worse clinical outcomes [28].

Previous experimental models have suggested that interventions targeting mitochondrial homeostasis, such as sirtuin-1 and peroxisome proliferator-activated receptor gamma coactivator 1 alpha activation, may protect against β-cell apoptosis in septic conditions [29]. It is plausible that the beneficial effects observed in this study involve modulation of similar pathways, although further molecular analyses are required to confirm this hypothesis. Additionally, the observed reductions in histological

inflammation and necrosis may reflect decreased infiltration of macrophages and neutrophils, which are key effectors in LPS-induced tissue injury [30].

Despite the promising results observed in this study, several limitations should be acknowledged. First, the relatively short duration of exposure and sacrifice time point may not fully capture the long-term effects of RF and PM therapies. Second, the study does not assess downstream molecular mediators such as sirtuin 1, NF-κB, or mitochondrial enzymes, which would further elucidate the mechanistic basis of the observed protective effects. Third, since the tissues used in this study were obtained from a different experimental study, blood parameters related to the pancreas could not be evaluated. Fourth, while rat models provide valuable insights, extrapolation to human physiology should be approached cautiously.

In conclusion, the current findings demonstrate that RF and PM therapies, especially when combined, offer significant protection against LPS-induced pancreatic injury in a rat model of sepsis. These interventions restore islet morphology and endocrine hormone expression, potentially through anti-inflammatory and antioxidative mechanisms. This study paves the way for future research into non-invasive biophysical therapies as adjunctive treatments for organ protection in systemic inflammatory conditions such as sepsis.

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Authors contributions: S.T., O.K., H.A and O.O. have constructed/constructed the main idea and hypothesis of the study. They developed the theory and arranged/edited the material and method section. S.T. and O.O. has/have done the evaluation of the data in the Results section. Discussion section of the article. Written by S.T, H.A, and O.O. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.

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Table 1. An explanation of the histolopatholohical scores

Score	**Description**
0	No degenerated cells
1	One to three degenerated cells
2	Four to seven degenerated cells
3	More than eight degenerated cells

Table 2. Statistical *p* values of pancreatic histopathology and IHC scores among groups

	Adjusted *p* Values						
Groups	**Hyperemia**	**Edema**	**Infiltration**	**Degeneration**	**Insulin**	**Glucagon**	**Amylin**
Con and LPS	<0.001	0.006	<0.001	<0.001	<0.001	<0.001	<0.001
Con and RF	0.497	0.351	0.404	0.179	<0.001	<0.001	<0.001
Con and PM	0.926	0.351	0.975	0.381	<0.001	<0.001	<0.001
Con and PM+RF	0.994	0.351	0.761	0.991	>0.999	0.910	0.297
LPS and RF	<0.001	0.351	0.041	0.002	<0.001	<0.001	<0.001
LPS and PM	<0.001	0.351	0.002	<0.001	<0.001	<0.001	<0.001
LPS and PM+RF	<0.001	0.351	0.009	<0.001	<0.001	<0.001	<0.001
RF and PM	0.926	>0.999	0.761	0.991	<0.001	<0.001	<0.001
RF and PM+RF	0.277	>0.999	0.975	0.381	<0.001	<0.001	<0.001
PM and PM+RF	0.744	>0.999	0.975	0.656	<0.001	<0.001	<0.001

Tukey's multiple comparisons test. IHC: Immunohistochemistry, Con: Control
LPS: Lipopolysaccharide, RF: Radiofrequency, PM: Pulsed magnetic field

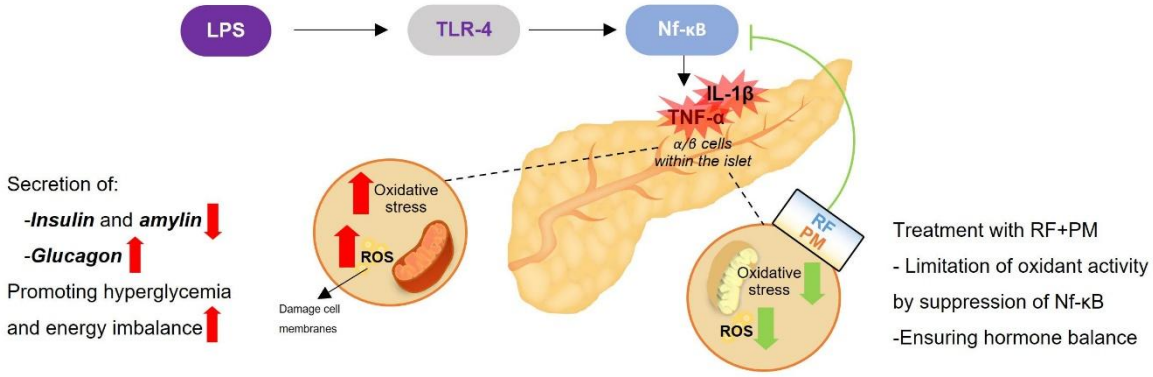

Figure 1. The potential effects of RF and PM treatments on pancreatic islet function in LPS-induced sepsis

LPS: Lipopolysaccharide, RF: Radiofrequency, PM: Pulsed magnetic field, ROS: Reactive oxygen species, NF-κB: Nuclear factor kappa-light-chain-enhancer of activated B cells, TNF-α: Tumor necrosis factor alpha, TLR-4: Toll-like receptor 4, IL-1β: Interleukin-1 beta

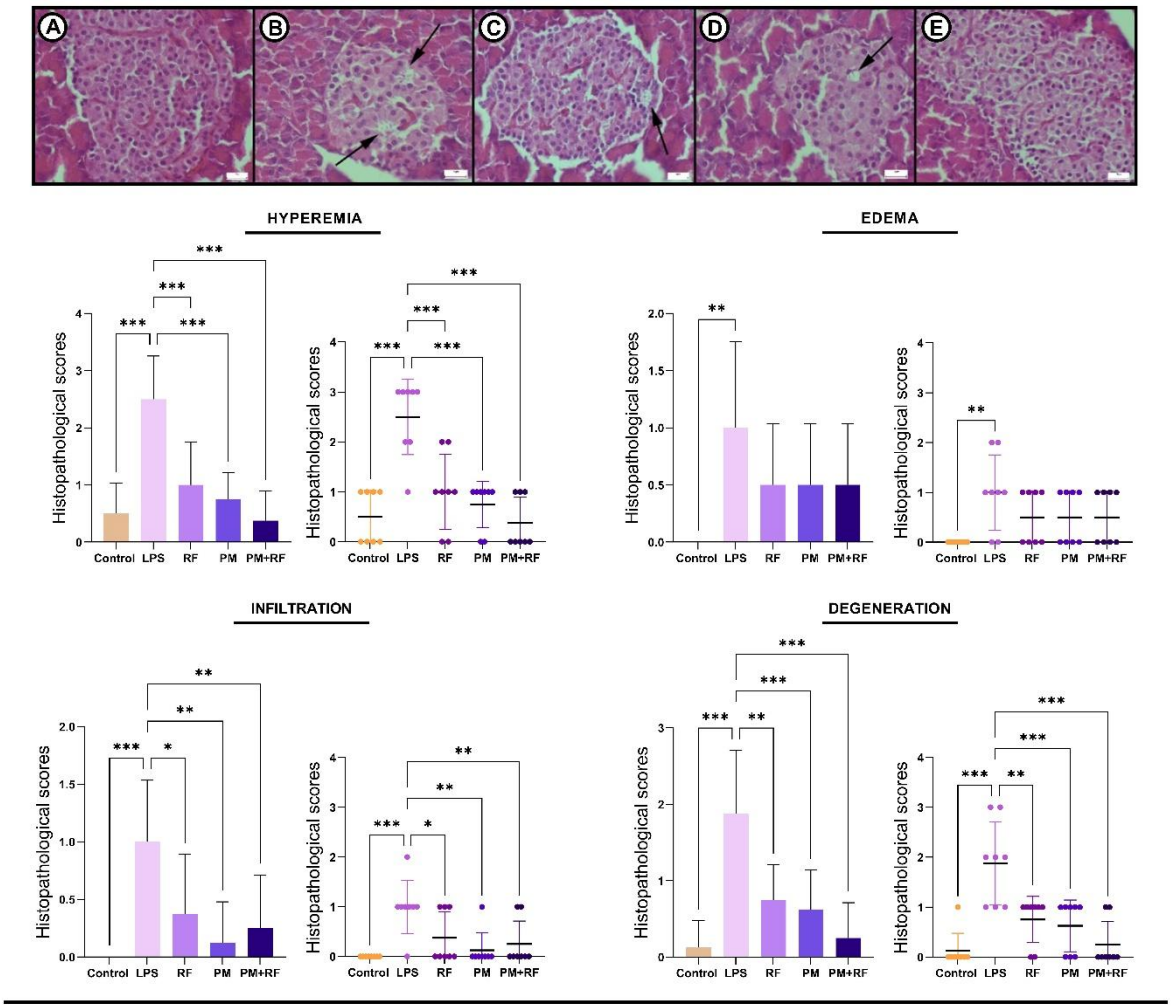

Figure 2. Representative immunohistochemical images and scoring evaluation of pancreatic tissue across experimental groups

(A) Control group: Normal pancreatic architecture with intact islets of Langerhans. (B) LPS group: Pronounced vacuolization within islet cells (arrows), indicating severe degenerative changes. (C) RF group: Reduced degenerative alterations compared to the LPS group. (D) PM group: Marked attenuation of histopathological damage. (E) PM+RF group: Nearly restored islet morphology, closely resembling normal histology. HE, scale bars=20 μm. Immunohistochemical scoring evaluation of tissues among groups by Tukey multiple comparison test. Data are expressed as mean ± standard deviation.

"*" represents $p<0.001$. LPS: Lipopolysaccharide, RF: Radiofrequency, PM: Pulsed magnetic field

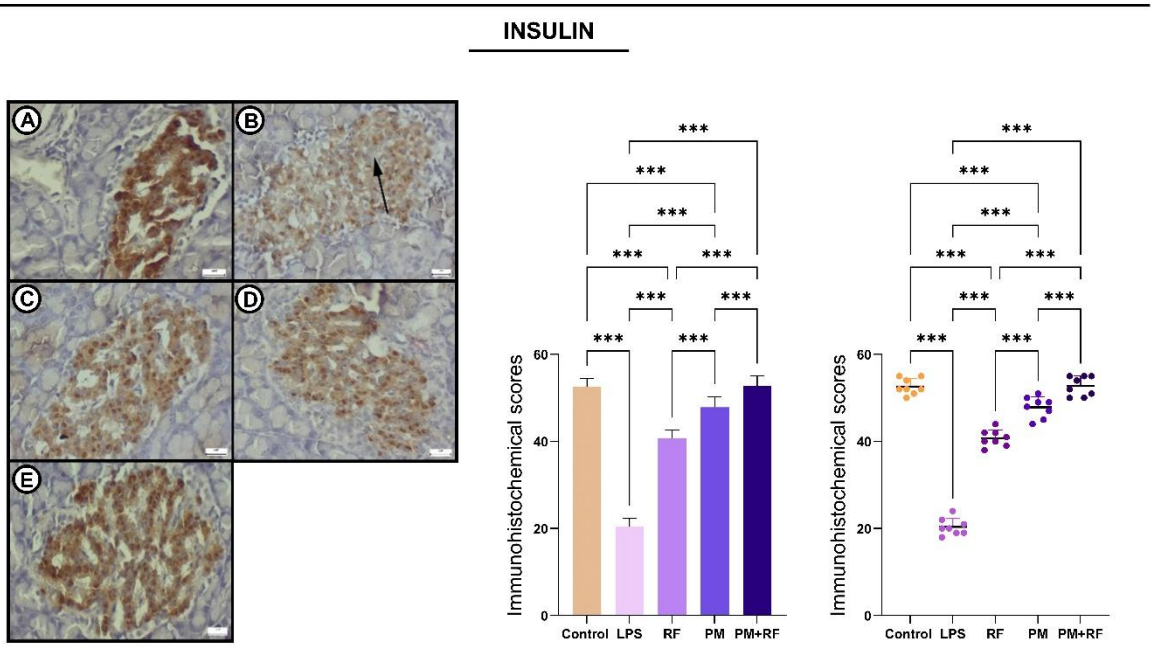

Figure 3. Representative immunohistochemical images and scoring evaluation of insulin expression in the islets of Langerhans across experimental groups

(A) Control group: Strong central immunoreactivity for insulin expression, indicating normal islet architecture. (B) LPS group: Marked reduction in insulin expression. (C) RF group: Mild restoration of in insulin expression (arrows). (D) PM group: Moderate improvement in insulin immunoreactivity. (E) PM+RF group: Near-complete normalization of insulin expression patterns. Streptavidin biotin peroxidase method, Scale bars=20 µm. Immunohistochemical scoring evaluation of tissues among groups by Tukey multiple comparison test. Data are expressed as mean ± standard deviation.

"*" represents $p<0.001$. LPS: Lipopolysaccharide, RF: Radiofrequency, PM: Pulsed magnetic field

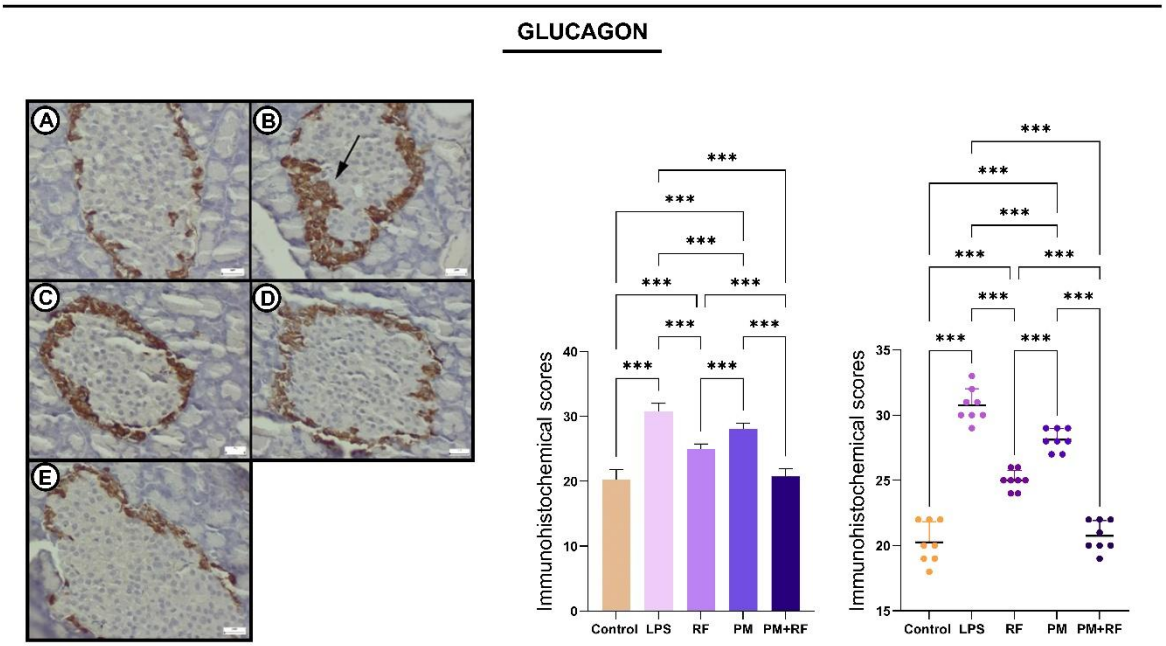

Figure 4. Representative immunohistochemical images and scoring evaluation of glucagon expression in the islets of Langerhans across experimental groups

(A) Control group: Mild peripheral glucagon expression, indicating normal islet architecture. (B) LPS group: Noticeable increase in glucagon-positive cells (arrows). (C) RF group: Decrease in glucagon-positive cells. (D) PM group: Reduction in glucagon expression. (E) PM+RF group: Near-complete normalization of glucagon expression patterns. Streptavidin biotin peroxidase method, Scale bars=20 µm. Immunohistochemical scoring evaluation of tissues among groups by Tukey multiple comparison test. Data are expressed as mean ± standard deviation.
"*" represents $p<0.001$. LPS: Lipopolysaccharide, RF: Radiofrequency, PM: Pulsed magnetic field

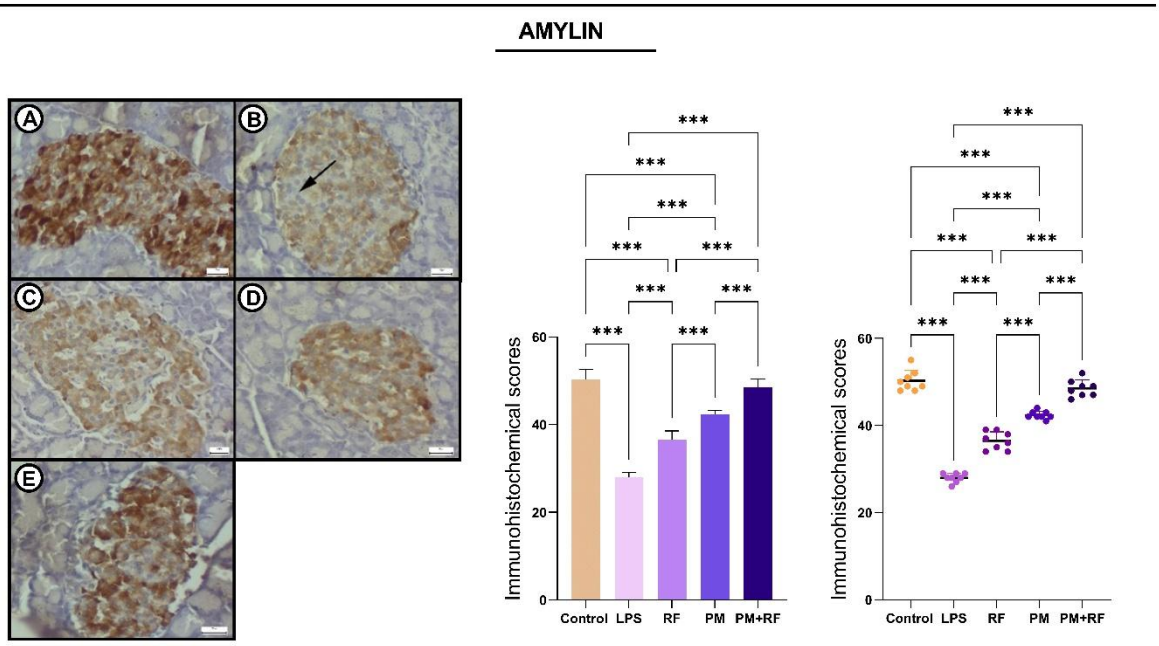

Figure 5. Representative immunohistochemical images and scoring evaluation of Langerhans across experimental groups

(A) Control group: Strong central immunoreactivity for amylin indicating normal islet architecture. (B) LPS group: Marked reduction in amylin expression (arrows). (C) RF group: Mild restoration of amylin expression. (D) PM group: Moderate improvement in amylin immunoreactivity. (E) PM+ RF group: Near-complete normalization of amylin expression patterns. Streptavidin biotin peroxidase method, Scale bars = 20 µm. Immunohistochemical scoring evaluation of tissues among groups by Tukey multiple comparison test. Data are expressed as mean ± standard deviation.

"*" represents $p<0.001$. LPS: Lipopolysaccharide, RF: Radiofrequency, PM: Pulsed magnetic field

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