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BASIC RESEARCH:

Protective Effect of Quinoa Extract on Periodontium and Serum YKL-40 Levels of Albino Rat Depression Model

Efecto protector del extracto de quinua sobre el periodonto y los niveles séricos de YKL-40 en un modelo de ratas albinas deprimidas

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ABSTRACT: The research was done to explore the influence of quinoa extract on periodontium, and to assess serum YKL-40 level in a depression rat model. An overall number of 30 male albino rats weighing170-180 g were used. Animals were grouped into three categories; group I: control group, group II: depressed group, group III: depressed group treated with 600 mg/kg body weight quinoa extract. The experimental duration extended to a period of 21 days. Blood samples obtained from the heart were transported to biochemistry tubes for ELISA analysis following euthanization. Mandibular molar region specimens were subjected to decalcification for histological evaluation. Quinoa extract ameliorated the degenerative changes of periodontium in the experimental depression model, increased body weight and serum serotonin level, and decreased serum cortisol and YKL-40 levels. Quinoa extract may be utilized as a preventative measure against the periodontal damage brought on by depression.

KEYWORDS: Depression; Periodontium; YKL-40; Quinoa extract.

RESUMEN: La investigación se realizó con el propósito de explorar la influencia del extracto de quinua sobre el periodonto y evaluar los niveles séricos de YKL-40 en un modelo de ratas en depresión. Se utilizaron un total de 30 ratas albinas macho con un peso de 170-180 gr. Los animales se dividieron en tres grupos: grupo I, control; grupo II, deprimido; y grupo III, deprimido tratado con extracto de quinua a una dosis de 600 mg/kg de peso corporal. El tiempo experimental se extendió por un período de 21 días. Tras la eutanasia, se obtuvieron muestras de sangre del corazón y se transfirieron a tubos para análisis bioquímico mediante ELISA. Las muestras de la región molar mandibular fueron sometidas a descalcificación para su evaluación histológica. El extracto de quinua mejoró los cambios degenerativos

del periodonto observados en el modelo experimental de depresión, incrementó el peso corporal y los niveles séricos de serotonina, y redujo los niveles séricos de cortisol y YKL-40. El extracto de quinua podría emplearse como una medida preventiva frente al daño periodontal inducido por la depresión.

PALABRAS CLAVE: Depresión; Periodonto; YKL-40; Extracto de quinua.

INTRODUCTION

Depression is well thought out as a major healthcare issue. Based on psychopathology, the consequences of depression differ from person to another, starting from reduced work efficiency, strained relationships with others, dietary and sleeping challenges, increased vulnerability to different illnesses, ending to suicide (1-3). 87% of patients with severe symptoms of depression had an intended suicidal attempt (4). The WHO reported in 2017 that the percentage of individuals suffering from depression had risen significantly over the previous ten years, with approximately 300 million affected people (5).

Plants have been utilized long ago for curing ailments. Their use as supplemental medicine has only increased throughout time due to their accessibility and affordability as healthcare substitutes (6, 7). Phytochemicals found in medicinal plants possess a variety of pharmacologic characteristics, involving anti-cancer, anti-diabetes and anti-inflammatory effects. They are beneficial to human wellness due to their variable biological impacts alongside their capability to regulate cell signaling pathways (8).

Quinoa's exceptional nutritional profile renders it one of the top dietary grains of the twenty-first century. In addition to protein with essential amino acids, it comprises substantial amounts of lipids, carbs, micro-minerals, and vitamins C, E, B2, B6, and B9 (9).

Quinoa encounters an extensive range of pharmaceutical traits including immune-modulatory, anti-diabetic, anti-microbial, and antioxidant functions (10). On the basis of previous experimental researches, quinoa suppressed the oxidative metabolite malondialdehyde, and raised the antioxidant enzymes glutathione, catalase, and superoxide dismutase (10, 11). Investigations suggested that the immune system was enhanced by the phenolic ingredients and saponins protein found in quinoa (12). Also, it may inhibit the expression of IL-8 and nuclear factor κB, which are both triggered by interleukin 1β (13).

YKL-40 is released from macrophages and neutrophils when stimulated by chondrocytes in arthritic inflammation (14). It is also secreted from vascular smooth muscle cells, endothelial (15) and embryonic cells (16). YKL-40 is known as a growth factor for connective tissue fibroblasts which triggers a chain of signals causing their proliferation. Meanwhile, it is an inflammatory marker that takes part in vascular mechanisms and inflammatory conditions (17). As well, YKL-40 is involved in the process of angiogenesis and in homeostasis-related pathological conditions (18, 19). It was documented that serum YKL-40 level increases during periodontitis and with its progression (20, 21). The primary motivation behind this study is the lack of information describing how quinoa extract administration affects periodontium and serum YKL-40 level in experimental depressionrats.

MATERIALS AND METHODS

EXPERIMENTAL ANIMALS

30 mature male albino rats weighing between 170 and 180 g were acquired from Future

University's animal house in Egypt.They were maintained in an appropriately aerated area with 24±1°C temperature, a 12 hour light and dark cycle, and an approximate humidity of 50±10%. Before testing, they were habituated for a week and nourished ordinary grain diet. The research was permitted by the Research Ethics Committee of Faculty of Oral and Dental Medicine, Future University (REC-FODM) number: FUE.REC (25)/4-2025.

SAMPLE SIZE CALCULATION

MedCalc® statistical program version 12.3.0.0 (MedCalc® software, Ostend, Belgium) was employed for calculating the sample size statistical calculator according to 95% confidence interval, and study power of 80% with 5% α error. Depending on the findings of a prior study, the null hypothesis could be rejected with a whole sample size of 10 (for each group) added to an additional 10 control groupsamples (22).

STUDY DESIGN

The rats were categorized into; group I (n=10) normal control (no medication), group II (n=10) depression group (induced depression without medication), group III (n=10) treated group (induced depression treated with quinoa extract).

Animalsof groups II and III were intraperitoneally injected with corticosterone at a daily dose of 20 mL/kg body weight (B.W.) (23) for 21 days to induce depression. One day after depression induction, 10 rats were treated with quinoa extract of dose 600 mg/kg BW by oral needle gavage every day for 21 days (24). By the end of the trial span, all animals were euthanized by administering 80 mg/kg sodium thiopental (EIPICO, Egypt) intraperitoneally preceding cervical dislocation. Heart blood samples were transported to testing tubes with gel and clot activator for ELISA analysis. Mandibular molar region specimens were subjected to decalcification for histological evaluation.

PREPARATION OF QUINOA EXTRACT

The plant powder extract production was accomplished in research labs of faculty of pharmaceutical science, Future University. A sample of 10 g. quinoa powder was normalized by 100 ml distilled water and 80% aqueous (v/v) ethanol liquid. The blend of ingredients was inserted in a revolving shaker for 24 h. The resultant solution was separated using Whatman N1 filter paper following 15 minutes spinning at 5000 g. A rotary evaporator was then used to make the filtrate purified and lyophilized. The obtained extract was preserved at a temperature of 4°C before being used (24).

HISTOLOGICAL EXAMINATION

To decalcify the specimens, they were soakedfor 4 weeks in 10% ethylene diamine tetra-acetic acid (EDTA) followed by dehydration and embedding in paraffin. Slices of 4-5µ thickness were stained by Hematoxylin and Eosin (H & E) for histopathological study.

BODY WEIGHT MEASUREMENTS

Experimental animals were measured for their B.W.at the beginning and at the end of the research.

BLOOD TEST FOR SEROTONIN, CORTISOL AND YKL-40 LEVEL MEASUREMENTS

Immediately after scarification, 4 ml of blood were drawn out by heart puncture in a standard plain vacutainer while all sterile procedures were followed. The blood was subjected to cooling (-4°C) and centrifugation at 4000 revolution/min. for 20 minutes. After the fluid was extracted and transferred to Eppendorf tubes, it was chilled at

-80°C until examination. Serotonin, cortisol and YKL-40 levels were examined in accordance with the guidelines provided by the manufacturer. An automated ELISA reader was employed to estimate the reaction by determining optical densitywith three readings for each sample.

STATISTICAL ANALYSIS

Data was provided as mean ± standard deviation (SD) in IBM SPSS Statistics 25 for Windows. The Shapiro-Wilk test was performed to approve that all information was in line with the normal distribution. ANOVA was carried out to assess the means of each group, while a "Tuckey" post hoc test was done to corroborate the results. Significant results were applied to the findings with a P-value lower than 0.05.

RESULTS

HISTOLOGICAL RESULTS:

GROUP I (CONTROL GROUP)

Normal histological configuration was displayed within the epithelium of the gingiva and underlying lamina propria (L.P). The keratinized stratified squamous gingival epithelium was recognized as basal, prickle, granular and keratinous cell layers. The epithelial ridges seemed uneven, innumerous, lengthy and slender (Figure 1.A).

The alveolo-dental group of periodontal ligament fibers was seen as regular abundant collagen bundles out spreading between cementum and bone. The majority of the fibers were obliquely directed pointing from cementum to bone (Figure 2.A).

Both cementum and alveolar bone exhibited ordinary staining character. Their boundaries appeared regular with evidence of Sharpey's fibers. Further, normal cementocytes and osteocytes were embedded within cementum and bone respectively (Figure 2.A).

GROUP II (DEPRESSION GROUP)

Noticeable histopathological alterations were marked in the epitheliumof the gingiva together with the L.P. The distinctive figure of the epithelial ridges was missed as they seemed broad and flattened. The basal cell layer showed detached areas of disintegrated basement membrane with absence of basal cell adhesion and regions of cellular hyperplasia. Moreover, vacuolated and swallowed prickle cells with flattened or degenerated nuclei were also identified. The granular cell layer appeared thin, while the keratinous layer was disrupted. The L.P displayed obvious degradation of collagen fibers and inflammatory cell infiltrate (Figure 1.B).

Depressed rats' jaw specimens revealed misplaced and deteriorated periodontal fibers accompanied by detached areas from the cementum and bone surfaces (Figure 2.B).

Cementum and alveolar bone appeared irregularly outlined, with difference in their staining character. Apparently, few empty lacunae as well as degenerated cementocytes and osteocytes were spotted together with absence of Sharpey's fibers (Figure 2.B).

GROUP III (DEPRESSED RATS TREATED WITH QUINOA EXTRACT

Group III specimens showed slender and long epithelial ridges with intact basement membrane. Some cells of the prickle layer seemed to be hypertrophied. The L.P revealed slight fibrous disintegration and apparent decline of inflammatory cell infiltration (Figure 1.C).

Jaw samples manifested dense obliquely directed periodontal fiber bundles with few focal

areas of degeneration. Alveolar bone revealed homogenous staining with irregular borders, while regular outlines were confined to cementum surface with attached Sharpey's fibers (Figure 2. C).

BODY WEIGHT RESULTS

Control group (group I) and depressed group treated with quinoa (group III) showed gain of weight with difference between the beginning and the end of the experiment of 24.228 g and 14.218 g respectively. Conversely, the depressed group (group II) revealed weight loss of average 15.169 g (Table 1, Figure 3).

BIOCHEMICAL RESULTS

CORTISOL SERUM LEVEL:

Group II showed the highest mean cortisol value, subsequently group III, while the lower most level was detected in group I. Significant difference was detected between whole groups (Table 2, Figure 4).

SEROTONIN SERUM LEVEL

The greatest serotonin level mean was recognized in group I, then group III. Group II exhibited the least value. Significant difference was detected between whole groups (Table 3, Figure 4).

YKL-40 SERUM LEVEL

Group II showed the highest mean YKL-40 serum value, afterward group I, whereas the least level was identified in group III. Significant difference was recognized between groups I and II, and between groups II and III, however, no significant difference could be spotted between groups I and III (Table 4, Figure 4).

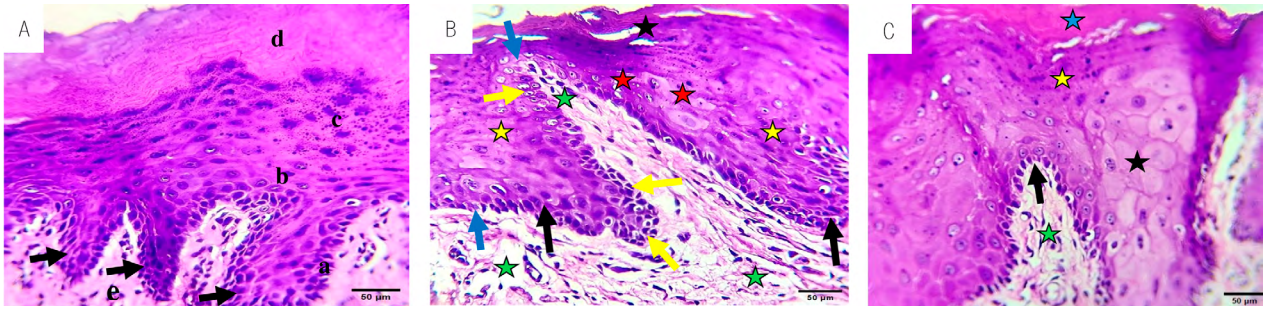

Figure 1. Photomicrograph of rat's gingiva: (A) group I showing: basal cell layer (a), prickle cell layer (b), granular cell layer (c), keratinous cell layer (d), numerous and slender epithelial ridges (arrows). (B) group II showing: broad and flattened epithelial ridges (black arrows), disintegration of the basement membrane (blue arrows), basal cellular hyperplasia (yellow arrows), vacuolated and swallowed prickle cells (red stars), flattened or degenerated nuclei (yellow stars), disrupted keratinous layer (black star), degradation of collagen fibers with inflammatory cell infiltration (green stars). (C) group III showing: long and slender epithelial ridges with intact basement membrane (black arrow), hypertrophied prickle cells (black star), normal granular cell layer (yellow star), normal keratinous layer (blue star), slight disintegration of collagen fibers (green star) (H&E, Orig. Mag.X 400).

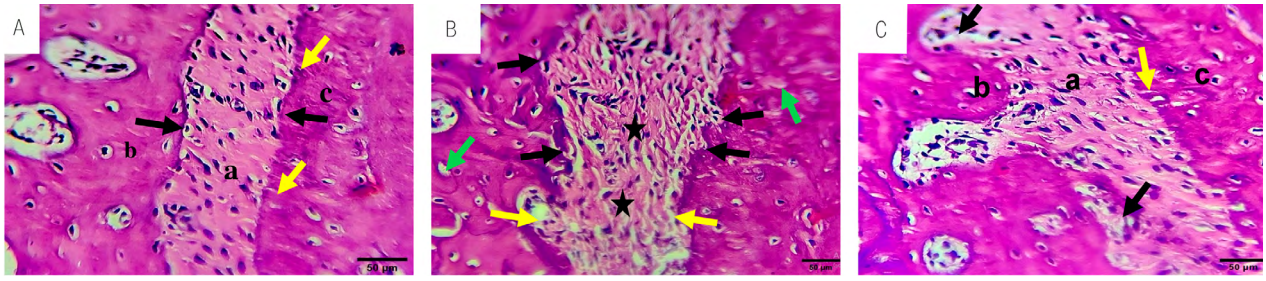

Figure 2. Photomicrograph of rat's periodontium: (A) group I showing: collagen bundles of oblique fibers (a), normal bone and osteocytes (b), normal cementum and cementocytes (c), regular boundaries of bone and cementum (black arrows), Sharpey's fibers (yellow arrows). (B) group II showing: misplaced and deteriorated periodontal fibers (black stars), detached areas from the cementum and bone surfaces (yellow arrows), irregular outlines of cementum and bone (black arrows), empty and degenerated cementocytes and osteocytes (green arrows). (C) group III showing: dense collagen bundles of oblique fibers (a), focal areas of periodontal degeneration (black arrows), normal bone and osteocytes with irregular borders (b), normal cementum, cementocytes and regular cemental outlines (c)with attached Sharpey's fibers (yellow arrow) (H&E, Orig. Mag.X 400).

Table 1. Average body weight for all groups at the beginning and the end of the experiment.

Groups	Average Body Weight		
	Beginning	End	Differences
Group I (Control)	176.347	200.575	24.228
Group II (Depressed)	174.887	159.718	-15.169
Group III (Quinoa- treated)	175.324	189.542	14.218

Figure 3. Bar chart representing average body weight for all groups at the beginning and at the end of the experiment.

Table 2. One-way ANOVA and Tukey's honestly significant difference (HSD) post-hoc test for pairwise comparison between groups regarding cortisol serum level.

Source	Sum of squares (SS)	Degrees of free-dom (df)	Mean square (MS)	F-statistic	p-value
Groups	103,760.82	2	51,880.41	188.6201	<0.001**
Error	7,426.41	27	275.0523		
Total	111,187.24	29			
Pairwise Comparisons		**Mean, μ ±SD,σ**		**Tukey HSD Q- statistic**	**Tukey HSD p-value**
GI (Control) *vs.* GII (Depressed)		μ1=357.314±10.4037 μ2=497.21± 20.769		26.6746	** p<0.01
GI (Control) *vs.* GIII (Quinoa-treated)		μ1=357.314±10.4037 μ3=397.497±16.8988		7.6619	** p<0.01
G II (Depressed) *vs.* GIII(Quinoa-treated)		μ2=497.21± 20.769 μ3=397.497±16.8988		19.0127	** p<0.01

** Significant factor at a level of significance, α=0.05.

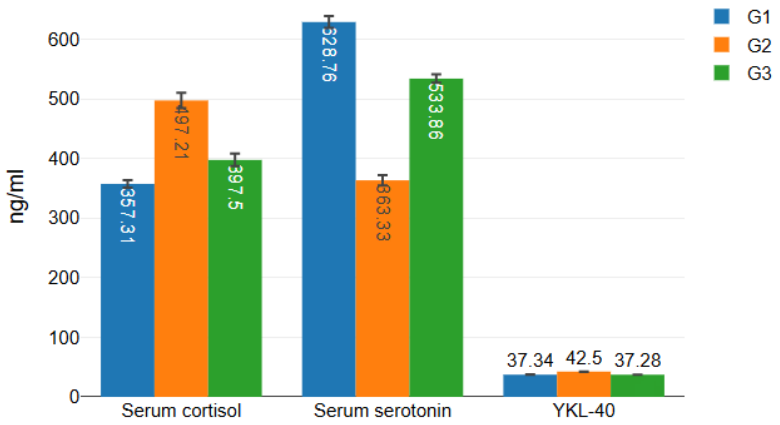

Figure 4. Bar chart representing mean ± SD of 10 observations regarding cortisol, serotonin and YKL-40 serum levels in each group.

Table 3. One-way ANOVA and Tukey's honestly significant difference (HSD) post-hoc test for pairwise comparison between groups regarding Serotonin serum level.

Source	Sum of squares (SS)	Degrees of free-dom (df)	Mean square (MS)	F-statistic	p-value
Groups	361,801.97	2	180,900.99	906.6771	<0.001**
Error	5,387.06	27	199.5209		
Total	367,189.04	29			
Pairwise Comparisons		**Mean, μ ±SD,σ**		**Tukey HSD Q- statistic**	**Tukey HSD p-value**
GI (Control) *vs.* GII (Depressed)		μ1=628.7642±16.2476 μ2=363.333 ±14.2409		59.4234	** p<0.01
GI (Control) *vs.* GIII (Quinoa-treated)		μ1=628.7642±16.2476 μ3=533.864±11.4792		21.2458	** p<0.01
G II (Depressed) *vs.* GIII(Quinoa-treated)		μ2=363.333 ±14.2409 μ3=533.864±11.4792		38.1777	** p<0.01

** Significant factor at a level of significance, α=0.05.

Table 4. One-way ANOVA and Tukey's honestly significant difference (HSD) post-hoc test for pairwise comparison between groups regarding YKL-40 serum level.

Source	Sum of squares (SS)	Degrees of free-dom (df)	Mean square (MS)	F-statistic	p-value
Groups	179.38	2	89.69	568.419	<0.001**
Error	4.2603	27	0.1578		
Total	183.6403	29			
Pairwise Comparisons		**Mean, μ ±SD,σ**		**Tukey HSD Q- statistic**	**Tukey HSD p-value**
GI (Control) *vs.* GII (Depressed)		μ1=37.336± 0.4297 μ2=42.497± 0.3907		41.0862	** p<0.01
GI (Control) *vs.* GIII (Quinoa-treated)		μ1= 7.336± 0.4297 μ3=37.284± 0.3689		0.414	0.899
G II (Depressed) *vs.* GIII(Quinoa-treated)		μ2=42.497±0.3907 μ3=37.284±0.3689		41.5002	** p<0.01

** Significant factor at a level of significance, α=0.05.

DISCUSSION

In our research, the influence of quinoa extract application on periodontium and serum YKL-40 level of depressed ratwas assessed. Experimental depression was induced by intraperitoneal injection of corticosterone (20 mL/kg BW) (23) once a day for 21 days.

Over the years, different animal models were designed to assess the effectiveness of new antidepressant medicines, and to assist clarify the pathophysiology behind depression (25). Adult male rats were the chosen research animals since they are effective models as clinical instances of depressive disorders, as well as to prevent any potential hormonal impacts associated with the gender of the female rats (26, 27).

Marked histological degenerative changes were spotted within group II rats' specimens. This goes hand in hand with previous researches confirming the deleterious effect of depression on various tissues such as lungs, nerves and salivary glands (28-30). These histopathological alterations may be brought on by the elevated serum corticosterone levels bringing on oxidative stress and release of reactive oxygen species. This contributes instantly to oxidative destruction of cell macromolecules (31), and subsequently resultant tissue destruction (30). However, the ameliorated histological features in group III rats may be the result of the strong antioxidant ability of its functional ingredients of phenolic compounds including flavonoids (32). Besides, certain quinoa peptides display radical scavenging capability plus suppression of lipid oxidation (33).

Group II rats revealed weight loss of 15.169 g, while group III showed gain of weight with difference between the beginning and the end of the experiment of 14.218 g. This suggests that when depressed rats are left untreated, their physical characteristics change and their psychomotor activities become weaker, which lowers their BW. According to the idea of depression, this is consistent with anhedonia, a state in which a depressed person tends to be lazy, lack desire and enthusiasm, and even lose his appetite, which leads to weight loss. The decrease in rats' body weight may be the consequence of rising cortisol levels and falling of serotonin owing to frequent corticosterone injections which results in depression. The increase in blood cortisol levels has various impacts on organ tissues and cells, including immunosuppressive, metabolic and catabolic processes (34). Moreover, elevated cortisol results in lipolysis and promotes the decomposing of tissue proteins (35). Quinoa comprises essential amino acids, antioxidants as well as inhibitors of phytate and enzymes (36-38). Following administration of quinoa extract, a significant fall in cortisol together with a significant rise in serotonin levels had been verified which explains weight gain. A number of studies have been accomplished supporting the reduction in cortisol levels caused by herbal medications (39, 40).

In the herein research, group II had the greatest mean YKL-40 value, whereas the lowest value was identified in group III. Kelesetal., outlined that YKL-40 serum concentration increased in patients suffering from periodontal inflammation. They declared that in order to assess the present condition of periodontitis, it might be required to check the amount of YKL-40 in body fluids previously and following periodontal remedy (20). Similar results were documented by Keles *et al.*, (21). The authors noted a substantial rise in YKL-40 level with an experimental indicator related to pocket depth, meaning that YKL-40 was linked to the degree of periodontitis (21). The reduction of serum YKL-40 level noticed in group III may be aconsequence of inflammation repression, since quinoa exhibits anti-inflammatory and antioxidant reactions(36).

Limitations of the herein investigation is that serumYKL-40 level was not evaluated before

inducing depression within the whole groups at the beginning of the experiment.

CONCLUSIONS

Depression caused destructive alterations in periodontium histology. It reduced BW and lowered serotonin serum levels. On contrary, it raised cortisol and YKL-40 concentrations. Treatment with quinoa extract improved the histopathology of periodontium and counteracted depression induced biochemical serum levels' changes. It is advised that toothpastes with varying concentrations of quinoa extract could be developed, and that additional research might be undertaken to find out how well these toothpastes offer protection against various periodontal conditions.

LIST OF ABBREVIATIONS: BW: Body weight. EDTA: ethylene diamine tetra-acetic acid. H & E: Hematoxylin and Eosin. IL: Interleukin. L.P: Lamina propria. SD: standard deviation.

AUTHOR CONTRIBUTION STATEMENT: Conceptualization and designing of the study: N.M.A.E; Methodology, Data analysis and interpretation: S.G. and M.E.D.; Writing-original draft preparation and revising the article: N.M.A.E, S.G. and M.E.D.; Final approval of the manuscript: N.M.A.E, S.G. and M.E.D.; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: N.M.A.E, S.G. and M.E.D.

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