

# Hereditary Polymorphism Of The Sodium-Uretic Peptides System And Long-Term Results Of Coronary Artery Stenting

Botir T. Daminov<sup>1</sup>, Bakhrom A. Alyavi<sup>2</sup>, Shuhrat I. Azizov<sup>3</sup>

<sup>1</sup>Rector of the Tashkent Pediatric Medical Institute, director of the RSSPMCP of Nephrology, Tashkent, Uzbekistan

<sup>2</sup>MD, professor assistant of Tashkent state dental institute, Tashkent, Uzbekistan.

<sup>3</sup>MD, professor assistant of Tashkent state dental institute, Tashkent, Uzbekistan.

Email: <sup>1</sup>mail@tashpmi.uz, <sup>2</sup>mail@tashpmi.uz, <sup>3</sup>mail@tashpmi.uz

## ABSTRACT

*The point of the study was to decide the impact of hereditary polymorphism on the impacts of endovascular revascularization in patients with coronary heart disease, angina pectoris FC III-IV.*

*The research included 158 patients with coronary heart disease with angina pectoris of FC III-IV pressure (ladies 34 -21.52%). Upon consideration within the ponder, all patients experienced: Echocardiography, TLC, genotyping of 6 genes of the system of natriuretic peptides, coronary angiography and stenting of the coronary courses. For follow-up examination, patients were welcomed after a year. The study included echocardiography, TLC, stress echocardiography.*

*Hereditary investigation permits foreseeing the drawn out impact of coronary supply route stenting: the overall danger of coronary illness movement (as stress-incited ischemia) in patients with minor alleles is 2.12 occasions higher than in patients with prevailing homozygotes for qualities of the natriuretic peptide system.*

*The current examination found that the presence of minor alleles of qualities of the arrangement of natriuretic peptides is related with a more prominent pervasiveness of atherosclerotic injuries of the coronary bed, the movement of underlying and useful rebuilding of the heart. What's more, the presence of minor alleles lessens the drawn out adequacy of coronary revascularization, both in the part of coronary atherosclerosis and in the part of the utilitarian condition of the myocardium (movement of LV dilatation and preservation of the sleeping myocardium).*

**KEY WORDS:** *stenting of coronary arteries, sodium urotic peptides, genetic polymorphism, stress echocardiography, myocardium, coronary bed.*

## 1. INTRODUCTION

Coronary illness is as yet the main source of death among grown-ups in many created nations (7 million per year). In the United States, around 1 million passages from coronary illness are recorded every year, of which roughly 160,000 are individuals 65 years old or more youthful [1]. 650 000 Europeans bite the dust each year from coronary illness, and AMI causes the passing of roughly 420 000 individuals [2]. After AMI, numerous patients are described by the presence of indications of angina pectoris, debilitated utilitarian state and an abatement in the personal satisfaction. The reformist nature of stenosing atherosclerosis, the

need to diminish high mortality, improve the personal satisfaction and increment the degree of social restoration of patients are an amazing motivation for finding better approaches to viably treat the sickness. The presentation of interventional medicines has become another page in the treatment of coronary vein illness.

Amidst the mind boggling injuries of CA, constant impediment is one of the most well-known and happens in roughly 15% of patients alluded for coronary angiography. Reestablishing the patency of the shuttle with the utilization of percutaneous coronary mediations can lessen the seriousness of angina pectoris, increment the contractile capacity of the myocardium and improve the anticipation. Correlation of patients with fruitful and ineffective PCI shows that the personal satisfaction and guess for effective mediation are essentially better [3,4]. It is realized that cardiovascular illnesses are multifactorial neurotic conditions dependent on complex pathogenesis that decides the development of an aggregate dependent on the association of hereditary elements with modifiable natural variables. Understanding the part of hereditary components in the turn of events and movement of cardiovascular breakdown permits you to investigate the etiology and pathogenesis of this illness. At long last, the hereditary examinations presently accessible for cardiological practice make it conceivable to unbiasedly assess the possibilities and adequacy of treatment, along these lines opening up additional opportunities for pharmacogenetics and pharmacogenomics that can give improved personal satisfaction and endurance of patients with cardiovascular breakdown [5,6]. Increasingly more proof shows that particular hereditary elements can prompt an adjustment in properties in the LLP quality framework, which influence the danger of cardio vascular disease and/or the reaction to sedate treatment. The point of the examination was to decide the impact of hereditary polymorphism on the impacts of endovascular revascularization in patients with coronary supply route illness, angina pectoris FC III-IV.

## 2. MATERIALS AND METHODS

The research included 158 patients with coronary illness with angina pectoris of FC III-IV pressure (ladies 34 - 21.52%). The normal period of patients is  $55.86 \pm 9.08$  years. All patients went through coronary angiography and just patients with signs for stenting of the coronary corridors were remembered for the investigation. The investigation and revascularization were done based on the Department of Interventional Cardiology of the RSSPCT and M. N. Semashko MR of the Ministry of Health of the Republic of Uzbekistan. The investigation did exclude patients with atrial fibrillation, intense febrile infections, end-stage organ disappointment, illnesses of different organs and frameworks requiring consistent essential treatment, patients with diabetes mellitus and thyroid sicknesses, harmful neoplasms, patients with contraindications for endovascular revascularization (ulcerative cycles in Gastrointestinal lot, hemorrhagic diathesis, ongoing kidney infection with an expected glomerular filtration pace of under 60 ml/min), patients with narrow mindedness to iodine-containing contrast specialists, patients who denied the endovascular system for individual reasons.

48 patients (30.38%) had post-infact cardio sclerosis among patients involved for the investigation. The rest of the patients, had no anamnestic and electrocardiographic indications of myocardial infarction. At the hour of incorporation in the investigation, all patients were taking standard fundamental treatment, including:- antiplatelet treatment: headache medicine - 152 patients (96.20%), clopidogrel - 6 patients (3.80%);- lipid-bringing down treatment: rosuvastatin 10-20 mg/day - 23 patients (14.56%), atorvastatin 20 mg/day - 82 patients (51.90%);- beta-blocker (bisoprolol, metoprolol, nebivolol) - 142 patients (89.88%);- calcium station blocker: verapamil 240 mg/day - 12 patients (7.59%), amlodipine - 46 patients

(29.11%);- angiotensin changing over compound inhibitors (enalapril, rimipril, perindopril, lisinopril) - 64 patients (40.51%);- angiotensin II receptor blocker (valsartan, losartan, telmisartan) - 28 patients (17.72%);- antiarrhythmics (amiodarone) - 27 patients (17, 09%);- diuretics (furosemide, torasemide, spironolactone) - 49 patients (31.01%);- isosorbide mono/dinitrate - 142 patients (89.88%). Upon consideration in the examination, all patients went through: Echocardiography, TLC, genotyping of 6 qualities of the arrangement of natriuretic peptides, coronary angiography and stenting of the coronary veins. After the strategy, patients were given proposals on fundamental treatment (twofold antiplatelet treatment, rosuvastatin 20 mg/day, beta-blocker/calcium station blocker if there should be an occurrence of contraindications to beta-blockers in independently chose portions, angiotensin changing over catalyst inhibitors/angiotensin antagonistic receptor inhibitors on account of antiarrhythmic, diuretics and nitrates as per signs) and the heading for perception by a cardiologist at the spot of residence. For subsequent assessment, patients were welcomed following a year. The examination included echocardiography, TLC, stress echocardiography. During measurable handling, intergroup correlations of the underlying and useful condition of the heart before revascularization and in the long haul (1 year) and contrasts in the overall elements of the patients were contemplated.

### *Echocardiography*

Echocardiography was done on a ultrasound scanner furnished with an arched cardiological sensor with a recurrence of 2-4 MHz. The examination was directed lying on the left side and on the back. Examining was completed utilizing standard echocardiography positions and projections. The accompanying boundaries were resolved:

- last diastolic volume of the left ventricle;- LV discharge part (EF);- sphericity file;
- Index of infringement of provincial contractility;
- index of systolic myocardial renovating;- e 'a' proportion of the paces of diastolic relocation in the period of the early and late diastole of the parallel edges of the mitral (for LV) and tricuspid (for pancreas) valves;
- LV myocardial mass list (LVMI);- Tei-basic list of the working of the ventricular myocardium;- The correct ventricle (pancreas);
- systolic weight in the aspiratory vein Pressure sticking in the pneumonic supply route;
- TAPSE - level of apical systolic removal of the horizontal edge of the tricuspid valve ring.

Stress Echocardiography study was performed with dynamic actual work utilizing the TMT technique, Bruce profile, stage term - 3 minutes. During the test, the elements of the discharge portion and the list of infringement of territorial contractility were contemplated. The example was deciphered as the presence of stress-instigated ischemia in case of ECG or clinical standards for ischemia, a lessening in the launch part, or an expansion in the record of infringement of provincial contractility. The resting myocardium was analyzed based on a diminishing in the record of infringement of territorial contractility against the foundation of the heap. The typical outcome is an expansion in the launch division against the foundation of the heap without changing the record of infringement of local contractility. Six-minute walk test. The patient was approached to stroll at the quickest movement for 6 minutes. In case of a stop, time tallying proceeded. Assessed distance traveled. The investigation of quality polymorphisms was completed at the high innovation focus of the Academy of Sciences of the Republic of Uzbekistan under the authority of Turdikulova Sh.U. in the science research center. Genotyping was done by polymerase chain response (PCR). To examine single nucleotide transformations (SNPs), 6 polymorphisms were chosen. The presence of minor alleles and allelic genotypes of 6 SNP qualities NPPA and NPPB was determined All given information was gone into Excell synopsis tables. After the arrangement of the groups, all boundaries were depicted as the number juggling mean and its standard deviation. The

dependability of intergroup contrasts was resolved utilizing Student's measure. On account of various correlations, the Student rule was remedied by the Bonferroni revision. An examination of the recurrence of event of signs between bunches was done utilizing the plain Chi-square measure and checking its dependability as per the tables relying upon the quantity of levels of opportunity.

### 3. RESULTS AND DISCUSSION

Taking into consideration the low recurrence of event of minor alleles during the investigation (Fig. 1), we built up a scale for evaluating hereditary polymorphism (Table 1), as per which a patient was doled out 1 point for each homozygous prevailing genotype, 2 focuses for each heterozygous genotype, each homozygous minor aggregate - 3 focuses, that is, a scoring portrays the presence and number of minor alleles. The amount of scores for every one of the 6 loci decided the scoring of hereditary polymorphism for 6 qualities of the system of natriuretic peptides. By far most of patients in this examination demonstrated a score of 6 (113 individuals - 71.52%), in 45 patients (28.48%), the score was higher, showing the presence of minor alleles (Fig. 2).

**Table 1. Scale of genetic polymorphism. Studied allelic SNP genotypes of the NPPA and NPPB genes in the study group and their frequency (%)**

SNP	Homo-zygotic Dominant Allele	Score	Hetero-zygotic allele	Score	Homo-zygotic minor allele	Score
rs5068	CC 94,94%	1	CT 5,06%	2	TT 0%	3
rs198388	CC 94,30%	1	CT 4,43%	2	TT 1,27%	3
rs198389	TT 94,30%	1	TC 5,70%	2	CC 0%	3
rs5065	CC 89,87%	1	TC 8,23%	2	TT 1,90%	3
rs632793	AA 98,10%	1	AG 1,90%	2	GG 0%	3
rs198358	AA 89,87%	1	AG 10,13%	2	GG 0%	3

Polymorphism score = total points for all 6 genes

Figure 1. The frequency of occurrence of allelic genotypes of 6 SNP genes NPPA and NPPB in the studied group

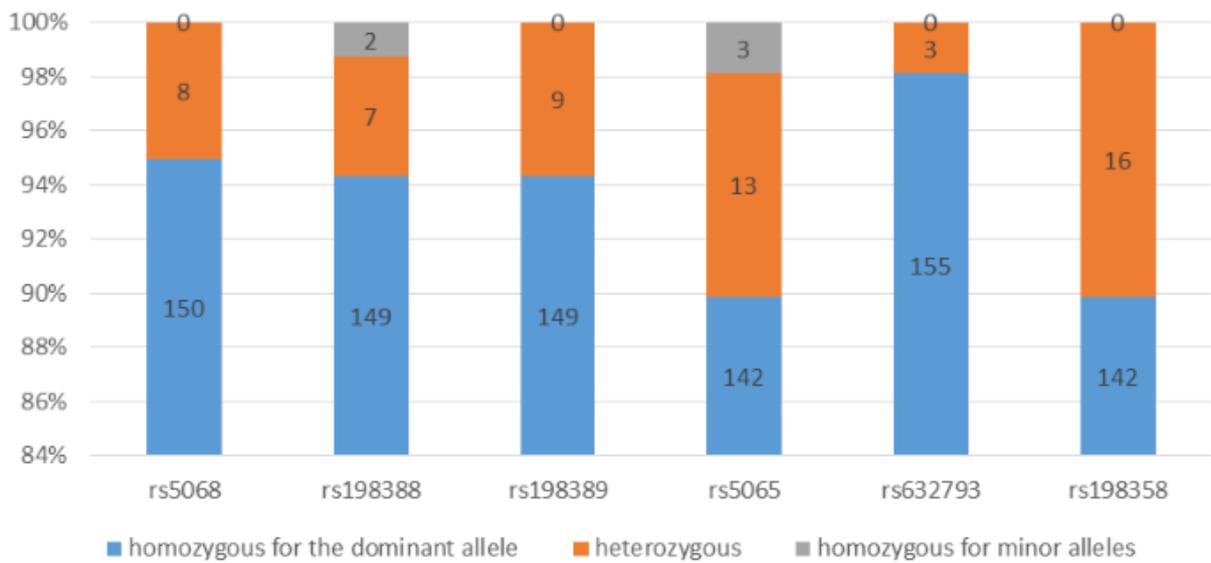
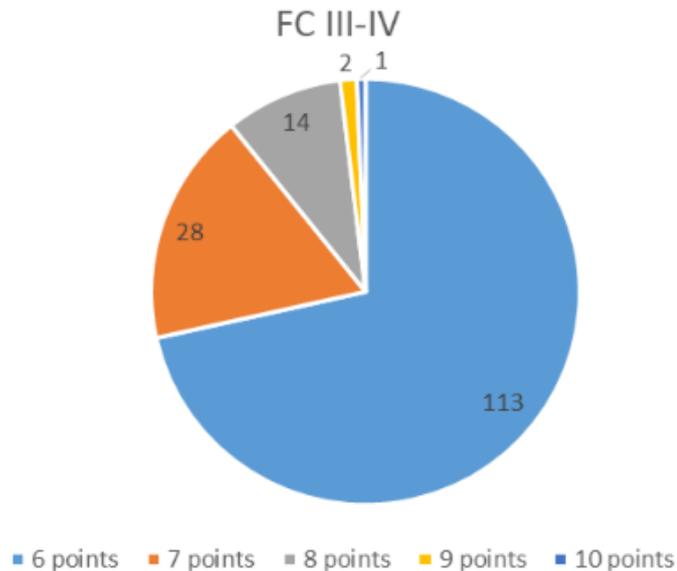


Figure 2. Frequency of occurrence of different points of genetic polymorphism in patients with angina pectoris



To contemplate the impact of hereditary polymorphism on the postponed consequences of endovascular coronary revascularization, all patients remembered for the examination were isolated into 2 gatherings: patients with a reviewed evaluation of hereditary polymorphism by 6 qualities of the uretic peptide framework 6, for example predominant homozygotes (115 patients) and with a ball a score higher than 6 focuses, that is, having at any rate 1 minor allele of the considered SNPs (50 patients). Correlation of these gatherings of patients demonstrated that by age these gatherings didn't vary from one another (Table 2). Coronaroangiography uncovered that the presence of minor alleles was related with an essentially more articulated sore of the coronary bed: the quantity of hemodynamically huge stenoses of the coronary supply routes was fundamentally higher in the gathering of patients

with a high score of hereditary polymorphism ( $p < 0.001$ ). Comparison of the echocardiographic boundaries uncovered that the presence of minor alleles of 6 considered qualities was related with an altogether more noteworthy seriousness of the cycles of neurotic underlying and useful rebuilding of the heart. Specifically, in this gathering of patients, contrasted and predominant homozygotes, essentially higher volumes of the left offices of the heart were noted ( $p < 0.001$ , the dependability of intergroup contrasts for the two markers), a huge estimation of the LV sphericity list ( $p < 0.001$ ). Additionally in this gathering of patients there was a higher list of debilitated local contractility ( $p < 0.001$ ), which relates to a more noteworthy number of coronary stenoses, and, likewise, a lower discharge portion ( $p < 0.001$ ) and a file of systolic myocardial renovating ( $p < 0.001$ ). One of the qualities of obsessive renovating was a critical expansion in the LV myocardial mass list in the gathering of patients with minor alleles ( $p < 0.001$ ).

The practical condition of the myocardium shows a more articulated debilitation of diastolic unwinding ( $p < 0.001$ ) and a more articulated disability of the adequacy of isometric working of the LV myocardium (Tei LV and absolute,  $p < 0.001$ ). An articulated infringement of the useful condition of the left heart chambers prompted an expansion in the degree of weight in the LA (systolic and wedging pressure in the pneumatic supply route,  $p < 0.001$ ) in patients with minor alleles of the examined qualities. Moreover, in this gathering of patients, there was a more articulated infringement of the systolic capacity of the pancreas (TAPSE,  $p < 0.001$ ) while keeping up different boundaries of the primary and practical condition of the correct heart. More articulated primary and practical renovating of the myocardium related with the presence of minor alleles, prompted a critical reduction somewhere out there went during TLC in this gathering of patients ( $p < 0.001$ ).

Stenting of the coronary arteries during the year added to factually huge, yet clinically immaterial positive converse myocardial rebuilding, equivalent in the two groups, with the exception of 2 parameters: and the end-diastolic volume of the LV in the two groups of patients expanded, which reflected the movement of obsessive renovating, more articulated in the gathering patients with an evaluation of the hereditary polymorphism of the natriuretic peptide arrangement of more than 6 (the general elements was  $5.43 \pm 9.56\%$  versus  $1.24 \pm 7.44\%$ ,  $p < 0.05$ ). Another pointer, the elements of which contrasted in the groups distinguished by the point gauge of hereditary polymorphism, is the provincial contractility problem record. It diminished in the two gatherings of patients, however undeniably in patients with a record of more than six, which is presumably connected with an enormous number of embedded stents ( $3.31 \pm 1.02$  versus  $1.20 \pm 0.28$ ,  $p < 0.001$ ). Investigation of echocardiography boundaries one year in the wake of stenting of coronary conduits in patients with angina pectoris III-IV of FC strain, contingent upon the presence of minor alleles, indicated that critical contrasts endure between bunches with more articulated neurotic primary and practical redesigning in the gathering of patients with minor alleles.

Table 2. Comparative characteristics and annual dynamics of echocardiographic characteristics in patients with angina pectoris III - IV FC against the background of stenting of coronary arteries depending on genetic polymorphism (numerator - indices of patients - homozygotes for the dominant allele ( $n = 113$ ) in the denominator - patients with minor alleles : heterozygotes or homozygotes for minor alleles ( $n = 45$ ))

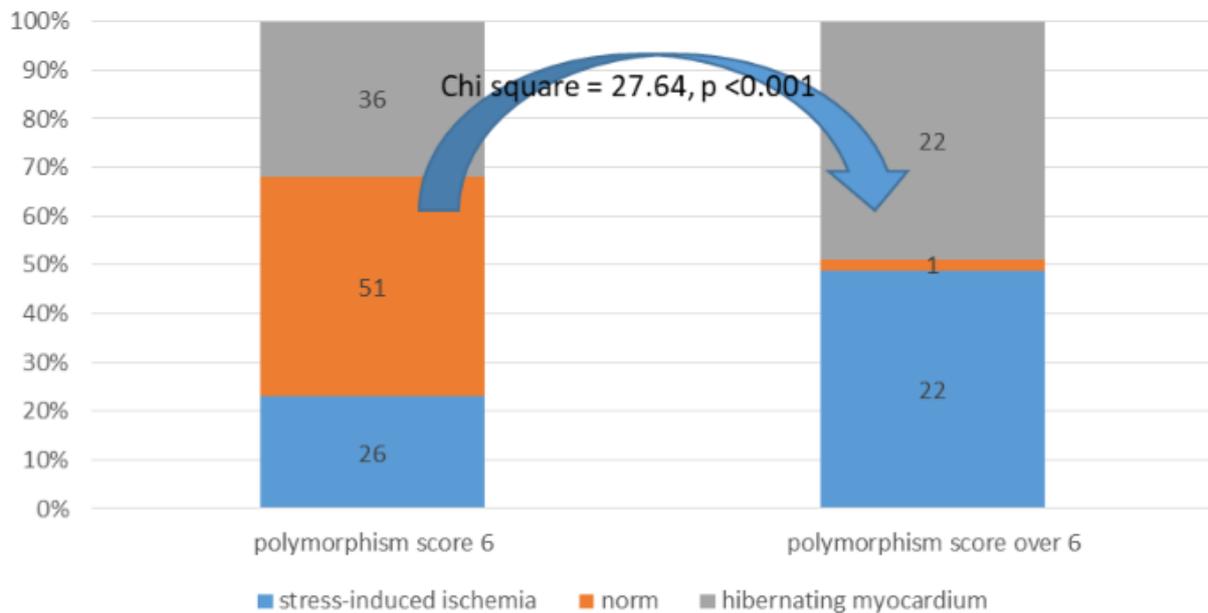
Index	Initially	12 months	Относительная динамика, %
The number of stenosis of the coronary arteries	$1,30 \pm 0,48$ $3,71 \pm 1,04^{^^^}$		
Age	$56,67 \pm 9,44$ $53,82 \pm 7,84$		
Systolic blood pressure, mmHg	$137,17 \pm 24,79$ $143,78 \pm 31,93$	$128,98 \pm 17,31^{***}$ $133,00 \pm 19,35^{**}$	$-4,75 \pm 9,94$ $-5,70 \pm 10,11$
Diastolic blood pressure, mmHg	$88,32 \pm 16,47$ $92,00 \pm 20,95$	$82,74 \pm 11,74^{***}$ $84,89 \pm 13,08^{***}$	$-5,02 \pm 10,30$ $-5,89 \pm 10,43$
Heart rate in minutes	$79,08 \pm 15,01$ $77,20 \pm 14,29$	$77,88 \pm 15,22$ $76,82 \pm 12,59$	$-1,05 \pm 10,37$ $0,32 \pm 10,14$
Tshh, m	$461,87 \pm 56,86$ $255,29 \pm 54,65^{^^^}$	$537,70 \pm 159,19^{***}$ $280,53 \pm 88,19^{^^^*}$	$16,63 \pm 32,94$ $9,94 \pm 25,87$
ejection fraction, %	$57,31 \pm 3,51$ $47,53 \pm 2,56^{^^^}$	$59,33 \pm 5,66^{***}$ $51,00 \pm 6,31^{^^^*}$	$3,67 \pm 9,44$ $7,52 \pm 14,66$

ILP, ml / m <sup>2</sup>	$27,39 \pm 4,20$ $47,20 \pm 6,84^{^^^}$	$27,51 \pm 4,36$ $45,82 \pm 7,83^{^^^}$	$0,52 \pm 5,53$ $-2,50 \pm 12,15$
final LV diastolic volume, ml / m <sup>2</sup>	$95,39 \pm 8,99$ $120,22 \pm 12,49^{^^^}$	$96,34 \pm 8,99$ $126,78 \pm 17,71^{^^^*}$	$1,24 \pm 7,44$ $5,43 \pm 9,56^{\wedge}$
LV sphericity index, rel.	$0,76 \pm 0,12$ $1,18 \pm 0,27^{^^^}$	$0,77 \pm 0,20$ $1,21 \pm 0,15^{^^^}$	$0,42 \pm 16,98$ $5,39 \pm 17,42$
index of violation of regional contractility, score	$1,05 \pm 0,07$ $1,26 \pm 0,07^{^^^}$	$1,04 \pm 0,06^{**}$ $1,23 \pm 0,08^{^^^*}$	$-0,84 \pm 3,21$ $-2,42 \pm 4,54^{\wedge}$
myocardial systolic remodeling index, units	$77,69 \pm 16,66$ $41,72 \pm 7,25^{^^^}$	$82,01 \pm 21,73^{**}$ $42,81 \pm 7,51^{^^^}$	$5,69 \pm 18,60$ $7,09 \pm 41,61$
e'/a' ЛЖ, отн ед	$0,88 \pm 0,18$ $0,45 \pm 0,14^{^^^}$	$0,90 \pm 0,18^{***}$ $0,47 \pm 0,16^{^^^*}$	$3,11 \pm 7,77$ $4,78 \pm 14,31$
LV myocardial mass index, g / m <sup>2</sup>	$119,44 \pm 9,44$ $151,53 \pm 16,32^{^^^}$	$119,75 \pm 10,76$ $149,51 \pm 17,50^{^^^}$	$0,30 \pm 5,05$ $-1,23 \pm 6,30$
Tei LV Rel.	$0,37 \pm 0,04$ $0,54 \pm 0,08^{^^^}$	$0,35 \pm 0,06^{***}$ $0,51 \pm 0,10^{^^^*}$	$-5,06 \pm 10,98$ $-4,61 \pm 11,36$
Right ventricle, cm	$2,61 \pm 0,48$ $2,60 \pm 0,45$	$2,62 \pm 0,46$ $2,58 \pm 0,44$	$0,72 \pm 5,10$ $-0,54 \pm 2,20^{\wedge}$
TAPSE mm	$15,96 \pm 2,37$ $8,53 \pm 1,85^{^^^}$	$16,57 \pm 2,67^{***}$ $8,89 \pm 2,07^{^^^*}$	$3,90 \pm 8,83$ $4,54 \pm 10,99$
e' / a' RV, rel.	$0,82 \pm 0,39$ $0,88 \pm 0,43$	$0,87 \pm 0,37^{**}$ $0,90 \pm 0,38$	$13,15 \pm 43,70$ $12,61 \pm 51,90$
Jamming pressure in the pulmonary artery, mmHg	$16,49 \pm 2,08$ $24,49 \pm 2,90^{^^^}$	$16,04 \pm 2,27^{***}$ $23,91 \pm 3,10^{^^^*}$	$-2,68 \pm 6,79$ $-2,37 \pm 4,94$
pulmonary systolic pressure, mmHg	$26,10 \pm 1,80$ $34,31 \pm 2,33^{^^^}$	$25,65 \pm 2,22^{***}$ $33,67 \pm 2,65^{^^^*}$	$-1,73 \pm 4,50$ $-1,87 \pm 4,05$
Tei RV, отн ед	$0,38 \pm 0,10$ $0,39 \pm 0,10$	$0,37 \pm 0,10^{***}$ $0,38 \pm 0,10^*$	$-2,13 \pm 4,57$ $-2,63 \pm 5,89$
total Tei, rel	$0,75 \pm 0,10$ $0,93 \pm 0,12^{^^^}$	$0,73 \pm 0,11^{***}$ $0,89 \pm 0,14^{^^^*}$	$-3,67 \pm 5,61$ $-3,83 \pm 8,04$

than 6 and 26 patients (23.01 %) in the gathering with a score of 6 (chi-square = 10.02,  $p < 0.01$ ). Curiously, the marvel of myocardial hibernation was likewise more frequently distinguished in patients with minor alleles of the contemplated qualities of the natriuretic peptide framework (22 patients - 48.89% versus 36 patients - 31.86%, chi-square = 3.97,  $p < 0.05$ ).

Consequently, hereditary investigation permits foreseeing the drawn out impact of coronary corridor stenting: the general danger of coronary course illness movement (as stress-actuated ischemia) in patients with minor alleles is 2.12 occasions higher than in patients with

Figure 3. Frequency of various echocardiographic responses to dynamic physical activity one year after stenting of the coronary arteries depending on the presence of minor alleles of genes of systemic natriuretic peptides genes



relationship coefficients with gauge information and pointers toward the finish of the main year of development). This relationship is reasonable given the distinctions noted above between patients with and without minor alleles. The investigation of the connection between the overall elements of echocardiography and the evaluation of hereditary polymorphism uncovered huge positive associations with the elements and end-diastolic volume of the LV and launch part ( $p < 0.05$  for both relationship coefficients).

Table 3. Correlation coefficients of echocardiography and their dynamics during the year after stenting the coronary arteries with a genetic polymorphism score (critical values of the correlation coefficient for  $n > 100$ : 0.195 for a confidence level  $p < 0.05$ , 0.254 for a confidence level  $p < 0.01$ )

Indicators	Initially	12 months	Относительная динамика
Systolic blood pressure, mmHg	0,041117	0,045204	-0,0007
Diastolic blood pressure, mmHg	0,024314	0,019784	-0,00316
Heart rate in minutes	-0,04762	-0,02748	0,042303
Tshh, m	-0,84644**	-0,62298**	-0,11026
ejection fraction,%	-0,80534**	-0,48613**	0,236834*
ILP, ml / m2	0,874804**	0,838236**	-0,15987

final diastolic LV volume, ml / m <sup>2</sup>	0,813246**	0,811696**	0,220587*
LV sphericity ind, rel.	0,746204**	0,671425**	0,049146
index of violation of regional contractility, score	0,833982**	0,805216**	-0,1888
myocardial systolic remodeling index, units	-0,70807**	-0,61654**	0,127818
e' / a' LV, rel.	-0,77774**	-0,77432**	0,037537
LV myocardial mass index, g / m <sup>2</sup>	0,852533**	0,81017**	-0,08925
Tei LV Rel.	0,881372**	0,786446**	0,027374
Right ventricle, cm	-0,0308	-0,05444	-0,10649
TAPSE mm	-0,81285**	-0,78713**	0,052449
e' / a' RV, rel.	-0,01939	-0,04572	-0,01068
Jamming pressure in the pulmonary artery, mmHg	0,863524**	0,848759**	0,045974
систолическое давление в легочной артерии , мм.рт.ст	0,864744**	0,830257**	0,010131
Tei RV, отн ед	0,004744	0,001361	-0,03104
total Tei, rel	0,620695**	0,580541**	-0,00357

Note: \* - dependability of the connection coefficient. One character -  $p < 0.05$ , two characters -  $p < 0.01$

#### 4. CONCLUSION

In the current examination, it was discovered that the presence of minor alleles of the qualities of the natriuretic peptide framework is related with a more noteworthy commonness of atherosclerotic injuries of the coronary bed, the movement of primary and practical renovating of the heart. What's more, the presence of minor alleles decreases the drawn out adequacy of coronary revascularization both regarding coronary atherosclerosis and as far as the utilitarian condition of the myocardium (movement of LV dilatation and protection of resting myocardium).

#### CONFLICT OF INTERESTS AND CONTRIBUTION OF AUTHORS

The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article and report on the contribution of each author.

#### REFERENCES

- [1] Kant, N., Saralch, S., & Singh, H. (2011). Ponderomotive self-focusing of a short laser pulse under a plasma density ramp. *Nukleonika*, 56, 149-153.
- [2] Patyar, S., & Patyar, R. R. (2015). Correlation between sleep duration and risk of stroke. *Journal of Stroke and Cerebrovascular Diseases*, 24(5), 905-911.
- [3] Khamparia, A., & Pandey, B. (2015). Knowledge and intelligent computing methods in e-learning. *International Journal of technology enhanced learning*, 7(3), 221-242.
- [4] Singh, A., Lin, Y., Quraishi, M. A., Olasunkanmi, L. O., Fayemi, O. E., Sasikumar, Y., ... & Kabanda, M. M. (2015). Porphyrins as corrosion inhibitors for N80 Steel in 3.5% NaCl solution: Electrochemical, quantum chemical, QSAR and Monte Carlo simulations studies. *Molecules*, 20(8), 15122-15146.

- [5] Singh, S., Kumar, V., Upadhyay, N., Singh, J., Singla, S., & Datta, S. (2017). Efficient biodegradation of acephate by *Pseudomonas pseudoalcaligenes* PS-5 in the presence and absence of heavy metal ions [Cu (II) and Fe (III)], and humic acid. *3 Biotech*, 7(4), 262.
- [6] Mia, M., Singh, G., Gupta, M. K., & Sharma, V. S. (2018). Influence of Ranque-Hilsch vortex tube and nitrogen gas assisted MQL in precision turning of Al 6061-T6. *Precision Engineering*, 53, 289-299.
- [7] Prakash, C., Singh, S., Pabla, B. S., & Uddin, M. S. (2018). Synthesis, characterization, corrosion and bioactivity investigation of nano-HA coating deposited on biodegradable Mg-Zn-Mn alloy. *Surface and Coatings Technology*, 346, 9-18.
- [8] Feng, X., Sureda, A., Jafari, S., Memariani, Z., Tewari, D., Annunziata, G., ... & Sychrová, A. (2019). Berberine in cardiovascular and metabolic diseases: from mechanisms to therapeutics. *Theranostics*, 9(7), 1923.
- [9] Bashir, S., Sharma, V., Lgaz, H., Chung, I. M., Singh, A., & Kumar, A. (2018). The inhibition action of analgin on the corrosion of mild steel in acidic medium: A combined theoretical and experimental approach. *Journal of Molecular Liquids*, 263, 454-462.
- [10] Sidhu, G. K., Singh, S., Kumar, V., Dhanjal, D. S., Datta, S., & Singh, J. (2019). Toxicity, monitoring and biodegradation of organophosphate pesticides: a review. *Critical Reviews in Environmental Science and Technology*, 49(13), 1135-1187.
- [11] Nanda, V., & Kant, N. (2014). Enhanced relativistic self-focusing of Hermite-cosh-Gaussian laser beam in plasma under density transition. *Physics of Plasmas*, 21(4), 042101.
- [12] Kotla, N. G., Gulati, M., Singh, S. K., & Shivapooja, A. (2014). Facts, fallacies and future of dissolution testing of polysaccharide based colon-specific drug delivery. *Journal of Controlled Release*, 178, 55-62.
- [13] Farooq, R., & Shankar, R. (2016). Role of structural equation modeling in scale development. *Journal of Advances in Management Research*.
- [14] Singh, S., Ramakrishna, S., & Gupta, M. K. (2017). Towards zero waste manufacturing: A multidisciplinary review. *Journal of cleaner production*, 168, 1230-1243.
- [15] Mahla, S. K., Dhir, A., Gill, K. J., Cho, H. M., Lim, H. C., & Chauhan, B. S. (2018). Influence of EGR on the simultaneous reduction of NO<sub>x</sub>-smoke emissions trade-off under CNG-biodiesel dual fuel engine. *Energy*, 152, 303-312.
- [16] Nanda, V., Kant, N., & Wani, M. A. (2013). Self-focusing of a Hermite-cosh Gaussian laser beam in a magnetoplasma with ramp density profile. *Physics of Plasmas*, 20(11), 113109.
- [17] Kaur, P., Singh, S. K., Garg, V., Gulati, M., & Vaidya, Y. (2015). Optimization of spray drying process for formulation of solid dispersion containing polypeptide-k powder through quality by design approach. *Powder Technology*, 284, 1-11.
- [18] Sharma, D., & Saharan, B. S. (2016). Functional characterization of biomedical potential of biosurfactant produced by *Lactobacillus helveticus*. *Biotechnology Reports*, 11, 27-35.
- [19] Wani, A. B., Chadar, H., Wani, A. H., Singh, S., & Upadhyay, N. (2017). Salicylic acid to decrease plant stress. *Environmental Chemistry Letters*, 15(1), 101-123.
- [20] Mishra, V., Patil, A., Thakur, S., & Kesharwani, P. (2018). Carbon dots: emerging theranostic nanoarchitectures. *Drug discovery today*, 23(6), 1219-1232.
- [21] Kumar, V., Pitale, S. S., Mishra, V., Nagpure, I. M., Biggs, M. M., Ntwaeaborwa, O. M., & Swart, H. C. (2010). Luminescence investigations of Ce<sup>3+</sup> doped CaS nanophosphors. *Journal of alloys and compounds*, 492(1-2), L8-L12.

- [22] Pudake, R. N., Swaminathan, S., Sahu, B. B., Leandro, L. F., & Bhattacharyya, M. K. (2013). Investigation of the Fusariumvirguliformefvtox1 mutants revealed that the FvTox1 toxin is involved in foliar sudden death syndrome development in soybean. *Current genetics*, 59(3), 107-117.
- [23] Kapoor, B., Singh, S. K., Gulati, M., Gupta, R., & Vaidya, Y. (2014). Application of liposomes in treatment of rheumatoid arthritis: quo vadis. *The scientific world Journal*, 2014.
- [24] Haldhar, R., Prasad, D., & Saxena, A. (2018). Myristica fragrans extract as an eco-friendly corrosion inhibitor for mild steel in 0.5 M H<sub>2</sub>SO<sub>4</sub> solution. *Journal of Environmental Chemical Engineering*, 6(2), 2290-2301.
- [25] Bordoloi, N., Sharma, A., Nautiyal, H., & Goel, V. (2018). An intense review on the latest advancements of Earth Air Heat Exchangers. *Renewable and Sustainable Energy Reviews*, 89, 261-280.
- [26] Sharma, P., Mehta, M., Dhanjal, D. S., Kaur, S., Gupta, G., Singh, H., ... & Chellappan, D. K. (2019). Emerging trends in the novel drug delivery approaches for the treatment of lung cancer. *Chemico-biological interactions*, 309, 108720.
- [27] Goga, G., Chauhan, B. S., Mahla, S. K., & Cho, H. M. (2019). Performance and emission characteristics of diesel engine fueled with rice bran biodiesel and n-butanol. *Energy Reports*, 5, 78-83.
- [28] Umashankar, M. S., Sachdeva, R. K., & Gulati, M. (2010). Aquasomes: a promising carrier for peptides and protein delivery. *Nanomedicine: Nanotechnology, Biology and Medicine*, 6(3), 419-426.
- [29] Sharma, A., Shree, V., & Nautiyal, H. (2012). Life cycle environmental assessment of an educational building in Northern India: A case study. *Sustainable Cities and Society*, 4, 22-28.
- [30] Kaur, T., Kumar, S., Bhat, B. H., Want, B., & Srivastava, A. K. (2015). Effect on dielectric, magnetic, optical and structural properties of Nd-Co substituted barium hexaferrite nanoparticles. *Applied Physics A*, 119(4), 1531-1540.
- [31] Datta, S., Singh, J., Singh, S., & Singh, J. (2016). Earthworms, pesticides and sustainable agriculture: a review. *Environmental Science and Pollution Research*, 23(9), 8227-8243.
- [32] Vij, S., & Bedi, H. S. (2016). Are subjective business performance measures justified?. *International Journal of Productivity and Performance Management*.
- [33] Chawla, R., & Sharma, S. (2017). Molecular dynamics simulation of carbon nanotube pull-out from polyethylene matrix. *Composites Science and Technology*, 144, 169-177.
- [34] Prakash, C., & Uddin, M. S. (2017). Surface modification of  $\beta$ -phase Ti implant by hydroxyapatite mixed electric discharge machining to enhance the corrosion resistance and in-vitro bioactivity. *Surface and Coatings Technology*, 326, 134-145.
- [35] Saxena, A., Prasad, D., & Haldhar, R. (2018). Investigation of corrosion inhibition effect and adsorption activities of Cuscuta reflexa extract for mild steel in 0.5 M H<sub>2</sub>SO<sub>4</sub>. *Bioelectrochemistry*, 124, 156-164.
- [36] Prabhakar, P. K., Kumar, A., & Doble, M. (2014). Combination therapy: a new strategy to manage diabetes and its complications. *Phytomedicine*, 21(2), 123-130.
- [37] Wheeler, K. C., Jena, M. K., Pradhan, B. S., Nayak, N., Das, S., Hsu, C. D., ... & Nayak, N. R. (2018). VEGF may contribute to macrophage recruitment and M2 polarization in the decidua. *PLoS One*, 13(1), e0191040.
- [38] Singh, A., Lin, Y., Ansari, K. R., Quraishi, M. A., Ebenso, E. E., Chen, S., & Liu, W. (2015). Electrochemical and surface studies of some Porphines as corrosion inhibitor for J55 steel in sweet corrosion environment. *Applied Surface Science*, 359, 331-339.

- [39] Gill, J. P. K., Sethi, N., Mohan, A., Datta, S., & Girdhar, M. (2018). Glyphosate toxicity for animals. *Environmental Chemistry Letters*, 16(2), 401-426.
- [40] Kumar, V., Singh, S., Singh, J., & Upadhyay, N. (2015). Potential of plant growth promoting traits by bacteria isolated from heavy metal contaminated soils. *Bulletin of environmental contamination and toxicology*, 94(6), 807-814.
- [41] Patel, S. (2012). Potential of fruit and vegetable wastes as novel biosorbents: summarizing the recent studies. *Reviews in Environmental Science and Bio/Technology*, 11(4), 365-380.
- [42] Srivastava, G., Das, C. K., Das, A., Singh, S. K., Roy, M., Kim, H., ... & Philip, D. (2014). Seed treatment with iron pyrite (FeS<sub>2</sub>) nanoparticles increases the production of spinach. *RSC Advances*, 4(102), 58495-58504.
- [43] Nagpal, R., Behare, P. V., Kumar, M., Mohania, D., Yadav, M., Jain, S., ... & Henry, C. J. K. (2012). Milk, milk products, and disease free health: an updated overview. *Critical reviews in food science and nutrition*, 52(4), 321-333.
- [44] Vaid, S. K., Kumar, B., Sharma, A., Shukla, A. K., & Srivastava, P. C. (2014). Effect of Zn solubilizing bacteria on growth promotion and Zn nutrition of rice. *Journal of soil science and plant nutrition*, 14(4), 889-910.
- [45] Lin, Y., Singh, A., Ebenso, E. E., Wu, Y., Zhu, C., & Zhu, H. (2015). Effect of poly (methyl methacrylate-co-N-vinyl-2-pyrrolidone) polymer on J55 steel corrosion in 3.5% NaCl solution saturated with CO<sub>2</sub>. *Journal of the Taiwan Institute of Chemical Engineers*, 46, 214-222.
- [46] Mahesh, K. V., Singh, S. K., & Gulati, M. (2014). A comparative study of top-down and bottom-up approaches for the preparation of nanosuspensions of glipizide. *Powder technology*, 256, 436-449.
- [47] Singh, G., Gupta, M. K., Mia, M., & Sharma, V. S. (2018). Modeling and optimization of tool wear in MQL-assisted milling of Inconel 718 superalloy using evolutionary techniques. *The International Journal of Advanced Manufacturing Technology*, 97(1-4), 481-494.
- [48] Chauhan, C. C., Kagdi, A. R., Jotania, R. B., Upadhyay, A., Sandhu, C. S., Shirsath, S. E., & Meena, S. S. (2018). Structural, magnetic and dielectric properties of Co-Zr substituted M-type calcium hexagonal ferrite nanoparticles in the presence of  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> phase. *Ceramics International*, 44(15), 17812-17823.
- [49] Sharma, A., Shahzad, B., Kumar, V., Kohli, S. K., Sidhu, G. P. S., Bali, A. S., ... & Zheng, B. (2019). Phytohormones regulate accumulation of osmolytes under abiotic stress. *Biomolecules*, 9(7), 285.
- [50] Balakumar, P., Chakkarwar, V. A., Kumar, V., Jain, A., Reddy, J., & Singh, M. (2008). Experimental models for nephropathy. *Journal of the Renin-Angiotensin-Aldosterone System*, 9(4), 189-195.
- [51] Singh, A., Lin, Y., Liu, W., Kuanhai, D., Pan, J., Huang, B., ... & Zeng, D. (2014). A study on the inhibition of N80 steel in 3.5% NaCl solution saturated with CO<sub>2</sub> by fruit extract of *Gingko biloba*. *Journal of the Taiwan Institute of Chemical Engineers*, 45(4), 1918-1926.
- [52] Kaur, T., Kaur, B., Bhat, B. H., Kumar, S., & Srivastava, A. K. (2015). Effect of calcination temperature on microstructure, dielectric, magnetic and optical properties of Ba<sub>0.7</sub>La<sub>0.3</sub>Fe<sub>11</sub>Co<sub>0.7</sub>O<sub>19</sub> hexaferrites. *Physica B: Condensed Matter*, 456, 206-212.
- [53] Singh, P., Singh, A., & Quraishi, M. A. (2016). Thiopyrimidine derivatives as new and effective corrosion inhibitors for mild steel in hydrochloric acid: Electrochemical and quantum chemical studies. *Journal of the Taiwan Institute of Chemical Engineers*, 60, 588-601.

- [54] Anand, A., Patience, A. A., Sharma, N., & Khurana, N. (2017). The present and future of pharmacotherapy of Alzheimer's disease: A comprehensive review. *European journal of pharmacology*, 815, 364-375.
- [55] Saxena, A., Prasad, D., Haldhar, R., Singh, G., & Kumar, A. (2018). Use of *Sida cordifolia* extract as green corrosion inhibitor for mild steel in 0.5 M H<sub>2</sub>SO<sub>4</sub>. *Journal of environmental chemical engineering*, 6(1), 694-700.
- [56] Ahmadi, M. H., Ghazvini, M., Sadeghzadeh, M., Alhuyi Nazari, M., Kumar, R., Naeimi, A., & Ming, T. (2018). Solar power technology for electricity generation: A critical review. *Energy Science & Engineering*, 6(5), 340-361.
- [57] Kant, N., Wani, M. A., & Kumar, A. (2012). Self-focusing of Hermite–Gaussian laser beams in plasma under plasma density ramp. *Optics Communications*, 285(21-22), 4483-4487.
- [58] Gupta, V. K., Sethi, B., Upadhyay, N., Kumar, S., Singh, R., & Singh, L. P. (2011). Iron (III) selective electrode based on S-methyl N-(methylcarbamoyloxy) thioacetimidate as a sensing material. *Int. J. Electrochem. Sci*, 6, 650-663.
- [59] Mehta, C. M., Srivastava, R., Arora, S., & Sharma, A. K. (2016). Impact assessment of silver nanoparticles on plant growth and soil bacterial diversity. *3 Biotech*, 6(2), 254.
- [60] Gupta, V. K., Guo, C., Canever, M., Yim, H. R., Sraw, G. K., & Liu, M. (2014). Institutional environment for entrepreneurship in rapidly emerging major economies: the case of Brazil, China, India, and Korea. *International Entrepreneurship and Management Journal*, 10(2), 367-384.
- [61] Singh, A., Lin, Y., Obot, I. B., Ebenso, E. E., Ansari, K. R., & Quraishi, M. A. (2015). Corrosion mitigation of J55 steel in 3.5% NaCl solution by a macrocyclic inhibitor. *Applied Surface Science*, 356, 341-347.
- [62] Ansari, K. R., Quraishi, M. A., Singh, A., Ramkumar, S., & Obote, I. B. (2016). Corrosion inhibition of N80 steel in 15% HCl by pyrazolone derivatives: electrochemical, surface and quantum chemical studies. *RSC advances*, 6(29), 24130-24141.
- [63] Jnawali, P., Kumar, V., & Tanwar, B. (2016). Celiac disease: Overview and considerations for development of gluten-free foods. *Food Science and Human Wellness*, 5(4), 169-176.
- [64] Saggu, S., Sakeran, M. I., Zidan, N., Tousson, E., Mohan, A., & Rehman, H. (2014). Ameliorating effect of chicory (*Chichorium intybus* L.) fruit extract against 4-tert-octylphenol induced liver injury and oxidative stress in male rats. *Food and chemical toxicology*, 72, 138-146.
- [65] Bhatia, A., Singh, B., Raza, K., Wadhwa, S., & Katare, O. P. (2013). Tamoxifen-loaded lecithin organogel (LO) for topical application: development, optimization and characterization. *International Journal of Pharmaceutics*, 444(1-2), 47-59.
- [66] Singh, A., Lin, Y., Liu, W., Yu, S., Pan, J., Ren, C., & Kuanhai, D. (2014). Plant derived cationic dye as an effective corrosion inhibitor for 7075 aluminum alloy in 3.5% NaCl solution. *Journal of Industrial and Engineering Chemistry*, 20(6), 4276-4285.
- [67] Raza, K., Thotakura, N., Kumar, P., Joshi, M., Bhushan, S., Bhatia, A., ... & Katare, O. P. (2015). C60-fullerenes for delivery of docetaxel to breast cancer cells: a promising approach for enhanced efficacy and better pharmacokinetic profile. *International journal of pharmaceutics*, 495(1), 551-559.
- [68] Prabhakar, P. K., Prasad, R., Ali, S., & Doble, M. (2013). Synergistic interaction of ferulic acid with commercial hypoglycemic drugs in streptozotocin induced diabetic rats. *Phytomedicine*, 20(6), 488-494.

- [69] Chaudhary, A., & Singh, S. S. (2012, September). Lung cancer detection on CT images by using image processing. In *2012 International Conference on Computing Sciences* (pp. 142-146). IEEE.
- [70] Mishra, V., Bansal, K. K., Verma, A., Yadav, N., Thakur, S., Sudhakar, K., & Rosenholm, J. M. (2018). Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems. *Pharmaceutics*, *10*(4), 191.
- [71] Singh, A. (2012). Hydroxyapatite, a biomaterial: its chemical synthesis, characterization and study of biocompatibility prepared from shell of garden snail, *Helix aspersa*. *Bulletin of Materials Science*, *35*(6), 1031-1038.
- [72] Arora, S., & Anand, P. (2019). Binary butterfly optimization approaches for feature selection. *Expert Systems with Applications*, *116*, 147-160.
- [73] Chhikara, N., Kushwaha, K., Sharma, P., Gat, Y., & Panghal, A. (2019). Bioactive compounds of beetroot and utilization in food processing industry: A critical review. *Food Chemistry*, *272*, 192-200.
- [74] Singh, S., Kumar, V., Chauhan, A., Datta, S., Wani, A. B., Singh, N., & Singh, J. (2018). Toxicity, degradation and analysis of the herbicide atrazine. *Environmental chemistry letters*, *16*(1), 211-237.
- [75] Baranwal, T., & Pateriya, P. K. (2016, January). Development of IoT based smart security and monitoring devices for agriculture. In *2016 6th International Conference-Cloud System and Big Data Engineering (Confluence)* (pp. 597-602). IEEE.
- [76] Trukhanov, S. V., Trukhanov, A. V., Salem, M. M., Trukhanova, E. L., Panina, L. V., Kostishyn, V. G., ... & Sivakov, V. (2018). Preparation and investigation of structure, magnetic and dielectric properties of (BaFe<sub>11</sub>. 9Al<sub>0</sub>. 1O<sub>19</sub>) 1-x-(BaTiO<sub>3</sub>) x bicomponent ceramics. *Ceramics International*, *44*(17), 21295-21302.
- [77] Singh, S., Singh, N., Kumar, V., Datta, S., Wani, A. B., Singh, D., ... & Singh, J. (2016). Toxicity, monitoring and biodegradation of the fungicide carbendazim. *Environmental chemistry letters*, *14*(3), 317-329.
- [78] Bhyan, B., Jangra, S., Kaur, M., & Singh, H. (2011). Orally fast dissolving films: innovations in formulation and technology. *Int J Pharm Sci Rev Res*, *9*(2), 9-15.
- [79] Saxena, A., Prasad, D., Haldhar, R., Singh, G., & Kumar, A. (2018). Use of Saraca ashoka extract as green corrosion inhibitor for mild steel in 0.5 M H<sub>2</sub>SO<sub>4</sub>. *Journal of Molecular Liquids*, *258*, 89-97.
- [80] Panghal, A., Janghu, S., Virkar, K., Gat, Y., Kumar, V., & Chhikara, N. (2018). Potential non-dairy probiotic products—A healthy approach. *Food bioscience*, *21*, 80-89.
- [81] Kumar, D., Agarwal, G., Tripathi, B., Vyas, D., & Kulshrestha, V. (2009). Characterization of PbS nanoparticles synthesized by chemical bath deposition. *Journal of Alloys and Compounds*, *484*(1-2), 463-466.
- [82] Ansari, K. R., Quraishi, M. A., & Singh, A. (2015). Corrosion inhibition of mild steel in hydrochloric acid by some pyridine derivatives: an experimental and quantum chemical study. *Journal of Industrial and Engineering Chemistry*, *25*, 89-98.
- [83] Singh, P. S., Singh, T., & Kaur, P. (2008). Variation of energy absorption buildup factors with incident photon energy and penetration depth for some commonly used solvents. *Annals of Nuclear Energy*, *35*(6), 1093-1097.
- [84] Ansari, K. R., Quraishi, M. A., & Singh, A. (2015). Isatin derivatives as a non-toxic corrosion inhibitor for mild steel in 20% H<sub>2</sub>SO<sub>4</sub>. *Corrosion Science*, *95*, 62-70.
- [85] Singh, A., Lin, Y., Ebenso, E. E., Liu, W., Pan, J., & Huang, B. (2015). Gingko biloba fruit extract as an eco-friendly corrosion inhibitor for J55 steel in CO<sub>2</sub> saturated 3.5% NaCl solution. *Journal of Industrial and Engineering Chemistry*, *24*, 219-228.

- [86] Dey, A., Bhattacharya, R., Mukherjee, A., & Pandey, D. K. (2017). Natural products against Alzheimer's disease: Pharmaco-therapeutics and biotechnological interventions. *Biotechnology Advances*, 35(2), 178-216.
- [87] Ansari, K. R., Quraishi, M. A., & Singh, A. (2015). Pyridine derivatives as corrosion inhibitors for N80 steel in 15% HCl: Electrochemical, surface and quantum chemical studies. *Measurement*, 76, 136-147.
- [88] Patel, S. (2012). Threats, management and envisaged utilizations of aquatic weed *Eichhornia crassipes*: an overview. *Reviews in Environmental Science and Bio/Technology*, 11(3), 249-259.
- [89] Mia, M., Gupta, M. K., Singh, G., Królczyk, G., & Pimenov, D. Y. (2018). An approach to cleaner production for machining hardened steel using different cooling-lubrication conditions. *Journal of Cleaner Production*, 187, 1069-1081.
- [90] Kondrateva T.S. Biopharmaceutical studies of children's suppositories with phosphothiamine. Pharmacy.-Moscow, 1990.-No.5.-P.14-15.
- [91] Maksudova F.Kh., Karieva E.S., Tursunova M.Kh. Study of the pharmacological properties of the combined gel of sodium diclofenac and benzketozone /Infection, immunity and pharmacologists I.- Tashkent.-2015.-№5.C.160-163 /
- [92] Maksudova F. Kh., Karieva E. S. In vitro equivalence evaluation of diclofenac sodium generic medicinal preparation. // Pharmacy, a scientific and practical journal, special issue, St. Petersburg, 2016, pp. 461-464.
- [93] Piotrovsky V.K. Model and model-independent methods for describing pharmacokinetics: advantages, disadvantages and interrelation. // Antibiotics and medical biotechnology. -Moscow, 1997.-№7.P.492-497.
- [94] Kukes V.G., Sychev D.A. Clinical pharmacology. 5th ed., Moscow, 2017, p. 478.
- [95] Tillaeva U. M., Azizov U. M. Development of a methodology for isolating the amount of fensulcal determination from a biological object. Materials of the scientific-practical conference "Actual issues of education, science and production in pharmacy. Tashkent, 2009.-P.172 .
- [96] Tillaeva U.M. Standardization and quality control of fensulcal in soft dosage forms. // Authors' dissertation for the study of the academician of the candidate of pharmaceuticals. Sciences . Tashkent. 2011.23 s.
- [97] Golovkin V.A. On the importance of pharmacokinetics modeling for increasing the efficiency of biopharmaceutical research. // Optimization of drug supply and ways to increase the effectiveness of pharmaceutical science : Sat. Tez.dokl.-Kharkov, 1986.-P.61-62.
- [98] Stefanova A.V. Preclinical studies of medicines. Kiev. -2002. -650 p.
- [99] Briguori, C. Comparison of coronary drug-eluting stents versus coronary artery bypass grafting in patients with diabetes mellitus / C. Briguori, G. Condorelli, F. Airolidi et al. // Am. J. Cardiol. -2007. -Vol. 99. -P. 779-784
- [100] Akchurin R.S., Shiryayev A.A., Rudenko B.A. and others. Angiographic characteristics of invasive interventions. *Cardiological Bulletin* 2011, VI (VIII) 2. 37-45.
- [101] Bravata, D. M. Systematic review: the comparative effectiveness of percutaneous coronary interventions and coronary artery bypass graft surgery / D. M. Bravata, A. L. Gienger, K. M. McDonald et al. // *Ann. Intern. Med.* -2007. -Vol. 147. -P. 703-716.
- [102] Cohen, D. Three-year SYNTAX results extend CABG advantage to intermediate-risk patients / D. Cohen, A. P. Kappetein. -2010 // <http://www.Theheart.org>
- [103] Karpov Yu.A., Buza VV How to manage a patient after percutaneous coronary intervention? *Russian honey. Journal* 2011, 26, 1004-1007.

[104] Anstrom K.J., Kong D.F. et al. Clopidogrel use and longterm clinical outcomes after drug-eluting stent implantation. JAMA 2007, 297(2), 159-168.