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Optimization of Wear Parameters of Polyamide-6 Composite Materials Filled with Wollastonite Particles

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Abstract

Weight loss and friction coefficient prediction models for polyamide-6 (PA-6) composites filler with 0,5 and 10 wt.% wollastonite (W) particles was developed using Taguchi method by considering the parameters of sliding speed, applied load and filler ratio. The wear behavior of the specimen was investigated using pin-on-disc arrangement where the samples sliding against a AISI 4140 steel disk under different conditions. The wear tests were realized at the sliding speeds of 1.0, 1.5 and 2.0 ms-1 and under the loads of 6, 10, and 20 N. The obtained weight loss for with 5 and 10 wt.% wollastonite (W) particles PA-6 composites are lower than pure PA-6 weight loss under the same test conditions. The orthogonal array, signal-to-noise ratio (S/N) and analysis of variance (ANOVA) were employed to study the optimal testing parameters on composite samples. The estimated S/N ratio using the optimal testing parameters for specific wear rate were calculated and a good agreement was observed between the predicted and actual weight loss for a confidence level of 90%.

Keywords: Polyamide6, Wollastonite,Wear test, Optimization

1. Introduction

Polymer and polymer based composites are preferred for many industrial sectors such as automotive, electrical/electronic, aircraft and household applications. This is because these materials provide high strength/weight ratio in comparison to classic material and self-lubricant conditions. However, application areas of polymeric materials are restricted due to their low mechanical, thermal and tribological properties. Therefore reinforcements are used to increase their mechanical properties [1].

The used reinforcement and additive materials are glass fibre [2]; [3], CaCO3, [4];[5], kaolin, [6];[7], talc [8], wollastonite [9], and mica [10];[11] fillers and MoS2, graphite, carbon, wax, polytetrafluoroethylene (PTFE) and dry lubricants [12];[13]. Dry lubricants are materials which despite being in the solid phase, are able to reduce friction between two counterparts sliding against each other without the need for a liquid medium [14].

In engineering, PA was used for some components or parts of machines in chemical engineering, textile engineering, food processing, paper making industry, pharmacy, transportation engineering, agricultural engineering, coal and ceramic production, where PA-6 was substituted for carbon steel, stainless steel and bronze, because of its better anti-chemical-corrosion, water-repellent function, anti-adhesion, self-lubrication and higher impact resistance [15].

A relationship between the wear of the polymer matrix composites reinforcement and test parameters is desirable to obtain a better understanding of their wear behaviour. There have been numerous studies searching the influence of reinforcement, test conditions, contact geometry and environment on the tribological behaviour of polymer matrix.

Gordon and Kukureka [16] and Chen et al. [17] report that the friction coefficient can, generally, be reduced and the wear resistance increased by adding the reinforcement. Kim et al. [18], Yu et al. [19], Zhao et al. [20] and Samyn et al. [21], observed that the friction coefficient of polymers rubbing against metals decreases with the increase in load while Palabiyik and Bahadur [22] and Meng et al. [23] showed that its value increases with the increase in load.

In order to study the influence of AlB2 boride flakes on tribological properties of PA-6, PA-6 composites were produced by pressure moulding technique.

2. Experimental Procedures

2.1. Material

The composite specimens were prepared by screw in-line type injection molding machine. And the component of composite includes 0, 5, and 10 wt.% wollastonite (W) particles, respectively.

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2.2. Design of Experiments

The experiments are conducted per the standard orthogonal array. The selection of the orthogonal array is based on the condition that the degrees of freedom for the orthogonal array should be greater than, or equal to, the sum of the wear parameters. In this study, an L27 orthogonal array was chosen that has 27 rows and 13 columns, as shown in the Table 1.

Table 1. Orthogonal array L_{27} (3^{13}) of Taguchi design

L_{27} (3^{13}) test	1	2	3	4	5	6	7	8	9	10	11	12	13
1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	1	1	1	2	2	2	2	2	2	2	2	2	2
3	1	1	1	3	3	3	3	3	3	3	3	3	3
4	1	2	2	2	1	1	1	2	2	2	3	3	3
5	1	2	2	2	2	2	2	3	3	3	1	1	1
6	1	2	2	2	3	3	3	1	1	1	2	2	2
7	1	3	3	3	1	1	1	3	3	3	2	2	2
8	1	3	3	3	2	2	2	1	1	1	3	3	3
9	1	3	3	3	3	3	3	2	2	2	1	1	1
10	2	1	2	3	1	2	3	1	2	3	1	2	3
11	2	1	2	3	2	3	1	2	3	1	2	3	1
12	2	1	2	3	3	1	2	3	1	2	3	1	2
13	2	2	3	1	1	2	3	2	3	1	3	1	2
14	2	2	3	1	2	3	1	3	1	2	1	2	3
15	2	2	3	1	3	1	2	1	2	3	2	3	1
16	2	3	1	2	1	2	3	3	1	2	2	3	1
17	2	3	1	2	2	3	1	1	2	3	3	1	2
18	2	3	1	2	3	1	2	2	3	1	1	2	3
19	3	1	3	2	1	3	2	1	3	2	1	3	2
20	3	1	3	2	2	1	3	2	1	3	2	1	3
21	3	1	3	2	3	2	1	3	2	1	3	2	1
22	3	2	1	3	1	3	2	2	1	3	3	2	1
23	3	2	1	3	2	1	3	3	2	1	1	3	2
24	3	2	1	3	3	2	1	1	3	2	2	1	3
25	3	3	2	1	1	3	2	3	2	1	2	1	3
26	3	3	2	1	2	1	3	1	3	2	3	2	1
27	3	3	2	1	3	2	1	2	1	3	1	3	2

The wear parameters chosen for the experiments and their levels are shown in the Table 2. The experiment consists of 27 tests (each row in the L27 orthogonal array), and the columns are assigned to specific parameters. The first column is assigned to material type, the second column is assigned to sliding speed, and the fifth column is assigned to applied load, with the remaining columns assigned to their interactions (Figure1). The responses to be studied are the weight loss and friction coefficient of composite materials. The tests were replicated, resulting in a total of 81 tests, to allow the analysis of the variance of the results.

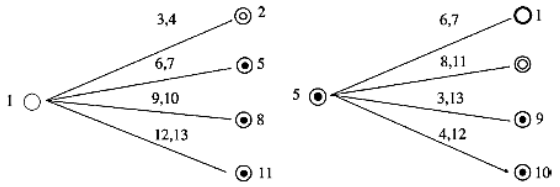

Figure 1. Linear graph L_{27} (3^{13}) [24]; [25].

Table 2. Test parameters with their values at three levels

Control factors	Level			
	I	II	III	Units
A:Material types	0	5	10	Wt.%
B:Sliding speed	1	1.5	2	m/s
C:Applied load	6	10	20	N

2.3. Experimental Set Up and Procedure

The pin-on-disc test apparatus shown in Figure 2 is used to investigate the dry sliding wear characteristics of the composite via the ASTM G99-95 standard. A wear specimen 6 mm in diameter and 10 mm in height is cut from samples, machined to size and then polished metallographically. The initial weight of the specimen is measured to 0.0001g. During the test the pin is pressed against the counterface AISI 4140 steel disc with a hardness of 56 HRC. After traversing a fixed D, the specimen is removed, cleaned with acetone, dried, and weighed to determine the mass loss due to wear. The difference in the mass before and after testing gives the dry sliding weight loss of the composite specimen.

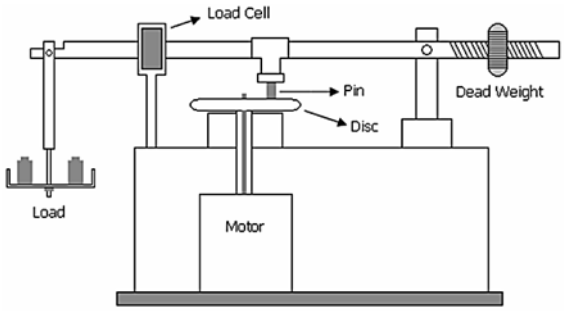

Figure 2. Schematic diagram of wear test rig

3. Results and Discussions

The plan of tests was developed with the aim of relating the influence of material types, sliding speed and applied load to determine weight loss and friction coefficient of composite materials. The statistical treatment of the data was made in two phases. The first phase was concerned with the effect of the factors and of the interactions and the ANOVA. The second phase allowed us to obtain the relations between the parameters.

3.1. Analysis of Factors

Analyses of the influence of each control factor (material types, sliding speed and applied load) on the weight loss and friction coefficient were performed with a so-called S/N response table, using a Minitab 16.1 computer package.

Table 3 shows the experimental plan and their results with calculated S/N ratios for weight loss and friction coefficient of the composites. The right side of the table included the results of the measured weight loss, friction coefficient and the calculated S/N ratio.

The response tables of the weight loss and friction coefficient are presented in Table 4 and 5. It indicates the S/N ratio at each level of control factor and how it was changed when settings of each control factor were changed from level 1 to level 3.

Table 3. Orthogonal array L27 (313) of Taguchi design

Material type	Sliding speed (m/s)	Applied load (N)	Weight Loss (mg)	S/N ratios (dB)	Friction coefficient	S/N ratios (dB)
PA6	1.0	6	0.00070	63.10	0.34	9.37
PA6	1.0	10	0.00075	62.50	0.48	6.38
PA6	1.0	20	0.00105	59.58	0.58	4.73
PA6	1.5	6	0.00085	61.41	0.26	11.70
PA6	1.5	10	0.00100	60.00	0.36	8.87
PA6	1.5	20	0.00120	58.42	0.57	4.88
PA6	2.0	6	0.00095	60.45	0.19	14.42
PA6	2.0	10	0.00125	58.06	0.24	12.40
PA6	2.0	20	0.00155	56.19	0.32	9.90
PA6+5%W	1.0	6	0.00055	65.19	0.13	17.72
PA6+5%W	1.0	10	0.00065	63.74	0.29	10.75
PA6+5%W	1.0	20	0.00090	60.92	0.41	7.74
PA6+5%W	1.5	6	0.00055	65.19	0.09	20.92
PA6+5%W	1.5	10	0.00085	61.41	0.15	16.48
PA6+5%W	1.5	20	0.00090	60.92	0.25	12.04
PA6+5%W	2.0	6	0.00075	62.50	0.05	26.02
PA6+5%W	2.0	10	0.00100	60.00	0.09	20.92
PA6+5%W	2.0	20	0.00105	59.58	0.12	18.42
PA6+10%W	1.0	6	0.00015	76.48	0.12	18.42
PA6+10%W	1.0	10	0.00050	66.02	0.18	14.89
PA6+10%W	1.0	20	0.00060	64.44	0.21	13.56
PA6+10%W	1.5	6	0.00035	69.12	0.07	23.10
PA6+10%W	1.5	10	0.00070	63.10	0.10	20.00
PA6+10%W	1.5	20	0.00085	61.41	0.13	17.72
PA6+10%W	2.0	6	0.00055	65.19	0.05	26.02
PA6+10%W	2.0	10	0.00080	61.94	0.06	24.44
PA6+10%W	2.0	20	0.00085	61.41	0.07	23.10

Table 4. The average S/N ratios (dB) response table for weight loss

Level	Material types	Sliding speed (m/s)	Applied Load (N)
1	59.97	64.66	65.40
2	62.16	62.33	61.86
3	65.46	60.59	60.32
Delta	5.49	4.07	5.09
Rank	1	3	2

The influence of interactions between control factors was also analyzed in the response table. Analysis of interactions between control factors could give very important additional information about the nature of the process under consideration. The control factor with the strongest influence was determined by differences values. The higher the difference, the more influential was the control factor or an interaction of two controls. It can be seen in Table 4, 5 that the strongest influence was exerted by material type, sliding speed and applied load, respectively.

Fig. 3-4(a) and (b) shows the main effects and their interaction plots for the weight loss and friction coefficient of the samples for S/N ratios.

Table 5. The average S/N ratios (dB) response table for friction coefficient

Level	Material types	Sliding speed (m/s)	Applied Load (N)
1	9.184	11.507	18.632
2	16.778	15.079	15.014
3	20.138	19.514	12.454
Delta	10.954	8.007	6.178
Rank	1	2	3

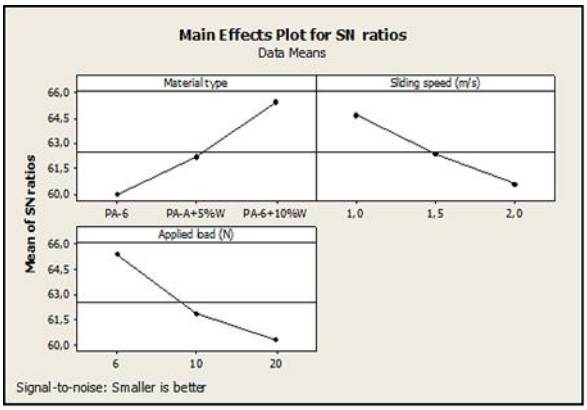

Figure 3(a).Plots for weight loss of samples: Main effects

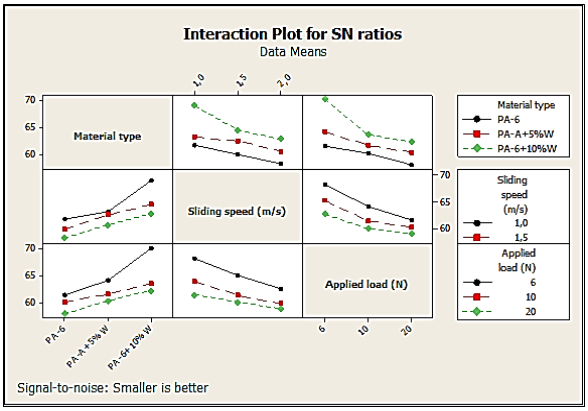

Figure 3(b). Plots for weight loss of samples: Interaction effects

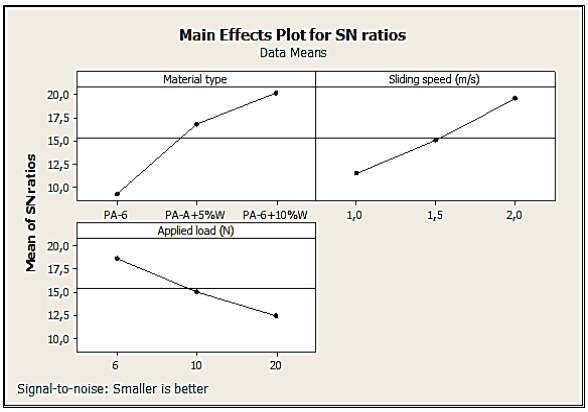

Figure 4(a). Plots for friction coefficient of samples: Main effects

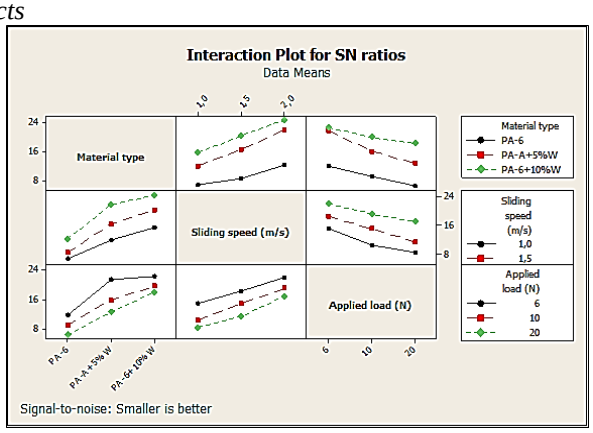

Figure 4(b). Plots for friction coefficient of samples: Interaction effects

The greater is the S/N ratio, the smaller is the variance of weight loss and friction coefficient around the desired value. Optimal testing conditions of these control factors could be very easily determined from the response graphs. The graphs show the change of the S/N ratio when the setting of the control factor was changed from one level to the other. The best weight loss and friction coefficient were at the higher S/N values in the response graphs.

It could be seen in Figure 3 that the initial optimum condition for the tested samples becomes A3B1C1 for main control factors of weight loss. This implies that in order to reduce the weight loss, the sliding speed and load should be lowered, while increasing the filler ratio. It is evident that Al+10%W composite material had the greatest effect on influence the optimal testing condition. In addition, the weight loss obviously increased as applied load increased from 6 to 20 N.

The response graph in Figure 4 clearly shows the optimum friction coefficient parameters are obtained at higher S/N ratios. Optimum test conditions for the friction coefficient become A3B3C1. The friction coefficient is found to decrease with sliding speed.

3.1.1.Anova

The analysis of variance (ANOVA) was used to investigate which design parameters significantly affect the quality characteristic. It was accomplished by separating the total variability of the S/N ratios, which is measured by sum of the squared deviations from the total mean S/N ratio, into contributions by each of the design parameters and the errors. Examination of the calculated values of Fishers (F) for all control factors also showed a very high influence of material types and low influence of sliding speed on weight loss of PA-6 composite materials (Table 4). The F value for each design parameters was calculated. Usually, when F > 4 it means that the design parameter showed a significant effect on the quality characteristic. Otherwise, other factors were neglected. The change of the interactions in the range given in Tables 6 had an insignificant effect on weight loss of materials because of the lower F value.

Table 6. Results of the ANOVA for weight loss

Source	***DF***	***SDQ***	***Variance***	***Test F***	F_{table}	***P[a](%)***
Material type	2	137.425	68.712	31.64	11.04[b]	34.41
Sliding speed (m/s)	2	75.109	37.554	17.3	11.04[b]	18.81
Applied load (N)	2	122.375	61.187	28.18	11.04[b]	30.64
Material type*Sliding speed	4	13.926	3.481	1.6	-	3.49
Material type*Applied load	4	26.391	6.597	3.04	-	6.61
Sliding speed*Applied load	4	6.778	1.694	0.78	-	1.70
Error	8	17.371	2.171			
Total	26	399.374				100

SDQ: sum of squares; DF: degrees of freedom; P: percentage of contribution
[a] percentage of contribution. [b] 99.5% confidence level.

The last column of the above table indicates the percentage of each factor contribution (P) on the total variation, thus exhibiting the degree of influence on the result. It may be observed in this table that the type of materials (P = 34.41 %), applied load (P = 30.64 %) and sliding speed (P = 18.81 %) had a significant influence on the weight loss. The interactions Material type*Sliding speed (P = 3.49 %), Material type*Applied load (P = 6.61 %) and Sliding speed*Applied load (P = 1.70 %) do not present percentages of physical significance of contribution on the weight loss of PA-6 composites.

Table 7. Results of the ANOVA for friction coefficient

Source	***DF***	***SDQ***	***Variance***	***Test F***	F_{table}	***P[a](%)***
Material type	2	566,898	283,449	1134,50	11.04[b]	52,89
Sliding speed (m/s)	2	289,632	144,816	579,62	11.04[b]	27,02
Applied load (N)	2	173,426	86,713	347,07	11.04[b]	16,18
Material type*Sliding speed	4	17,196	4,299	17,21	8.81[b]	1,60
Material type*Applied load	4	17,657	4,414	17,67	8.81[b]	1,65
Sliding speed*Applied load	4	4,997	1,249	5,00	3.84[c]	0,46
Error	8	1,990	0,248			
Total	26	1071,805				100

SDQ: sum of squares; *DF*: degrees of freedom; *P*: percentage of contribution, [a] percentage of contribution. [b] 99.5% confidence level. [c] 95% confidence level.

It can be observed from Table 7 that the material types (P= 52.89 %), the sliding speed (P = 27.02 %) and the applied load (P = 16.18 %) have great influence on the friction coefficient, the material types being the most prominent one. The interactions of Material type*Sliding speed (P = 1.60 %), Material type*Applied load (P = 1.65%) and Sliding speed*Applied load (P = 0.46 %) present significant percentage contributions on the friction coefficient. All the interactions do not present percentages of physical significance of contribution on the friction coefficient of PA-6 composites.

- The incorporation of wollastonite particles into PA-6 can either increase or reduce friction coefficient and reduce weight loss of the materials in sliding against AISI 4140 steel disc under dry sliding condition. The optimum wear resistance property was obtained at the wollastonite particle content of 10 wt.%.
- The friction coefficient of pure PA-6 and Wp/PA-6 composites increases with the increase of the load and decreases with the increase of the sliding speed.
- The weight loss of pure PA-6 and Wp/PA-6 composites increases with the increase of load and sliding speed.

4. Conclusions

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Mathematical modeling and analysis of tumor-immune system interaction by using Lotka-Volterra predator-prey like model with piecewise constant arguments

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Abstract

In this study, we present a Lotka-Volterra predator-prey like model for the interaction dynamics of tumor-immune system. The model consists of system of differential equations with piecewise constant arguments and based on the model of tumor growth constructed by Sarkar and Banerjee. The solutions of differential equations with piecewise constant arguments leads to system of difference equations. Sufficient conditions are obtained for the local and global asymptotic stability of a positive equilibrium point of the discrete system by using Schur-Cohn criterion and a Lyapunov function. In addition, we investigate periodic solutions of discrete system through Neimark-Sacker bifurcation and obtain a stable limit cycle which implies that tumor and immune system undergo oscillation.

Keywords: tumor growth, piecewise constant arguments, difference equation, stability

1. Introduction

Modeling tumor-immune interaction has attracted much attention in the last decades. This interaction is very complex and mathematical models can help to shape our understanding of dynamics this biological phenomenon. Most of the models consist of two main populations: tumor cells and effector cells such as hunting predator cells (Cytotoxic T lymphocytes) and resting predator cells (T-Helper cells) which are main struggle of immune system. Cytotoxic T lymphocytes (CTLs) responsible to kill tumor cells and resting predator cells account for to activity the native Cytotoxic T lymphocytes.

In order to describe tumor and effector cells interaction, many authors [1-16] have used Lotka-Volterra terms and logistic terms. While some of these models [1-9] consist of ordinary differential equations, the others [10-16] consist of delay differential equations. A familiar model included ordinary differential equations is constructed Kuznetsov and Taylor [1]. They have studied interaction between Cytotoxic T lymphocyte and immunogenic tumor and have obtained a threshold for the tumor growth. Kirschner and Panetta [2] have generalized this model to study the role of IL-2 in tumor dynamics. Another familiar tumor growth model has been proposed by Sarkar and Banerjee [3]. The model explains spontaneous tumor regression and progression under immunological activity.

On the other hand, there exists a discrete time delay in the mitosis phase (cell division phase) since tumor cells need a resting time for a proliferation. This biological phenomenon is explained much better by using delay differential equations instead of ordinary differential equations [10]. Therefore, many authors have considered delay differential equation included time delay factor for modeling tumor growth [10-16]. Sarkar and Banerjee [11] have constructed the model by using the time delay factor as follows:

$$\begin{cases} \dfrac{dM}{dt} = r_1 M\left(1-\dfrac{M}{k_1}\right) - \alpha_1 MN, \\ \dfrac{dN}{dt} = \beta NZ(t-\tau) - d_1 N - \alpha_2 MN, \\ \dfrac{dZ}{dt} = r_2 Z\left(1-\dfrac{Z}{k_2}\right) - \beta NZ(t-\tau) - d_2 Z, \end{cases} \quad (1)$$

where $M(t)$, $N(t)$ and $Z(t)$ are the number of tumor, hunting and resting cells respectively.

Since stability and bifurcations analysis of delay differential equations is more difficult, numerical analysis may be needed for such equations. In study [17], Cooke and Györi show that differential equation with piecewise constant arguments can be used to obtain good approximate solution of delay differential equations on the infinite interval $[0,\infty)$. Therefore, there has been great interest in studying differential equation with piecewise constant arguments which combine properties

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of both differential and difference equations [18-26]. I. Ozturk et al. [18] have modeled bacteria population by using differential equation

$$\frac{dx(t)}{dt} = rx(t)\{1 - \alpha x(t) - \beta_0 x(\llbracket t \rrbracket) - \beta_1 x(\llbracket t-1 \rrbracket)\}. \quad (2)$$

which includes both continuous and discrete time for a bacteria population.

These types of models also allow us to describe both microscopic and macroscopic level events that occur simultaneously. For the tumor-immune system interactions, microscopic interaction refers proliferation and activation of tumor cells together with their competition while macroscopic interaction refers to cancer invasion and metastases [27]. When one considers the both microscopic level interaction which needs a discrete time and macroscopic level interaction which needs continuous time simultaneously, there are two events in a population: a continuity and discrete time. Modeling tumor growth using differential equation with piecewise constant arguments, Bozkurt [19] have considered a more general case of equation (2) as follows:

$$\frac{dx(t)}{dt} = x(t)\{r(1 - \alpha x(t) - \beta_0 x([t]) - \beta_1 x([t-1])) + \gamma_1 x([t]) + \gamma_2 x([t-1])\}. \quad (3)$$

In the present paper, due to above biological facts, we replace the model (1) by adding piecewise constant arguments and get a system of differential equations

$$\begin{cases} \frac{dM}{dt} = r_1 M(t)\left(1 - \frac{M(t)}{k_1}\right) - \alpha_1 M(t)N(\llbracket t \rrbracket), \\ \frac{dN}{dt} = \beta N(t)Z(\llbracket t-1 \rrbracket) - d_1 N(t) - \alpha_2 M(\llbracket t \rrbracket)N(t), \\ \frac{dZ}{dt} = r_2 Z(t)\left(1 - \frac{Z(t)}{k_2}\right) - \beta N(\llbracket t \rrbracket)Z(t) - d_2 Z(t), \end{cases} \quad (4)$$

where $\llbracket t \rrbracket$ denotes the integer part of $t \in [0, \infty)$, $M(t)$, $N(t)$ and $Z(t)$ are the number of tumor, hunting and resting cells respectively. The parameter r_1 represents the growth rate and k_1 represents the maximum carrying capacity of tumor cells, r_2 is the growth rate and k_2 is the maximum carrying capacity of resting cells. The term $-d_1 N(t)$ is natural death of hunting cell. The competition term $-\alpha_1 M(t)N(\llbracket t \rrbracket)$ represents the loss of tumor cells due to encounter with hunting cells and $-\alpha_2 M(\llbracket t \rrbracket)N(t)$ represents the loss of hunting cells due to encounter with the tumor cells. The conversion rate from resting to hunting cells is represented parameter β. There exist a discrete delay time in this conversion which is represented term $Z(\llbracket t-1 \rrbracket)$. The term $\beta N(t)Z(\llbracket t-1 \rrbracket)$ represents growth of hunting T-cells and the term $-\beta N(\llbracket t \rrbracket)Z(t)$ represents loss of resting cells.

2. Local and global stabilty analysis of the system

An integration of each equation in system (4) on an interval $t \in [n, n+1)$, $n = 0,1,2,\dots$, give us

$$\begin{cases} \frac{dM}{dt} - M(t)\{r_1 - \alpha_1 N(n)\} = -r_1 K_1 \big(M(t)\big)^2, \\ \frac{dN}{N(t)} = \{\beta Z(n-1) - d_1 - \alpha_2 M(n)\}N(t)dt, \\ \frac{dZ}{dt} - Z(t)\{r_2 - \beta N(n) - d_2\} = -r_2 K_2 (Z(t))^2. \end{cases} \quad (5)$$

where $\frac{1}{k_1} = K_1$, $\frac{1}{k_2} = K_2$. If we solve each equations of system (5) and letting $t \to n+1$, we get a system of difference equations

$$\begin{cases} M(n+1) = \frac{M(n)[r_1 - \alpha_1 N(n)]}{[r_1 - \alpha_1 N(n) - r_1 K_1 M(n)]e^{-[r_1 - \alpha_1 N(n)]} + r_1 K_1 M(n)}, \\ N(n+1) = N(n)e^{\beta Z(n) - d_1 - \alpha_2 M(n)}, \\ Z(n+1) = \frac{Z(n)[r_2 - \beta N(n) - d_2]}{[r_2 - \beta N(n) - d_2 - r_2 K_2 Z(n)]e^{-[r_2 - \beta N(n) - d_2]} + r_2 K_2 Z(n)}. \end{cases} \quad (6)$$

In order to analysis system (6), we need to find positive equilibrium point of the system. If

$$\alpha_1 < \frac{4 d_1 K_2 r_1 r_2}{{d_2}^2 - 2 d_2 r_2 + {r_2}^2}, \quad \beta > \frac{d_1 K_1 K_2 r_2 + K_2 r_2 \alpha_2}{K_1 (r_2 - d_2)}, \quad (7)$$

$$K_1 > \frac{\alpha_2}{d_1} \text{ and } r_2 > d_2 \quad (8)$$

then, positive equilibrium point of the system is determined as $\bar{E} = (\bar{M}, \bar{N}, \bar{Z})$ where

$$\bar{M} = \frac{\beta^2 r_1 + \alpha_1(\beta d_2 - \beta r_2 + d_1 K_2 r_2)}{\beta^2 K_1 r_1 - K_2 r_2 \alpha_1 \alpha_2},$$

$$\bar{N} = \frac{r_1(-\beta K_1 d_2 + \beta K_1 r_2 - d_1 K_1 K_2 r_2 - K_2 r_2 \alpha_2)}{\beta^2 K_1 r_1 - K_2 r_2 \alpha_1 \alpha_2},$$

$$\bar{Z} = \frac{\beta(d_1 K_1 r_1 + r_1 \alpha_2) - (r_2 - d_2)\alpha_1 \alpha_2}{\beta^2 K_1 r_1 - K_2 r_2 \alpha_1 \alpha_2}.$$

The linearized system of (6) about positive equilibrium point $\bar{E}$ is $w(n+1) = Aw(n)$, where A is

$$A = \begin{pmatrix} e^{-K_1 r_1 \bar{M}} & -\frac{(1-e^{-K_1 r_1 \bar{M}})\alpha_1}{K_1 r_1} & 0 \\ -\alpha_2 \bar{N} & 1 & \beta \bar{N} \\ 0 & -\frac{(1-e^{-K_2 r_2 \bar{Z}})\beta}{K_2 r_2} & e^{-K_2 r_2 \bar{Z}} \end{pmatrix}. \quad (9)$$

The characteristic equation of matrix A is

$$p(\lambda) = (a_{11} - \lambda)[(1-\lambda)(a_{33} - \lambda) - a_{23}a_{32}] - a_{12}[a_{21}(a_{33} - \lambda)]. \quad (10)$$

Under the assumption

$$a_{11} = a_{55}, \quad (11)$$

an eigenvalue of (10) are computed as $\lambda_1 = e^{-K_1 r_1 \bar{M}} < 1$. Solving equation (11) with the fact $r_1 > r_2$ and considering inequalities (7) and (8) we have

$$\alpha_1 = \frac{\beta r_1 (K_1(-\beta r_1 + d_1 K_2 r_2) + K_2 r_2 \alpha_2)}{d_2(\beta K_1 r_1 - K_2 r_2 \alpha_2) + r_2(K_1(-\beta + d_1 K_2) r_1 - K_2 r_2 \alpha_2)}.$$

Thus, characteristic equation $p(\lambda)$ can be reduced second order equation

$$p_1(\lambda) = \lambda^2 + \lambda\left(-1 - e^{-K_1 r_1 \bar{M}}\right) + e^{-K_1 r_1 \bar{M}} + \frac{\bar{N}\left(1 - e^{-K_1 r_1 \bar{M}}\right)(\beta^2 K_1 r_1 - K_2 r_2 \alpha_1 \alpha_2)}{K_1 r_1 K_2 r_2} \quad (12)$$

Now we can determine stability conditions of discrete system (6) through the equation (12).

Theorem 1. Let $\bar{E}$ the positive equilibrium point of system (6). Suppose that

$$\alpha_1 = \frac{\beta r_1 (K_1(\beta r_1 - d_1 K_2 r_2) - K_2 r_2 \alpha_2)}{r_2(K_1(\beta - d_1 K_2) r_1 - K_2 r_2 \alpha_2)},$$

$$\frac{\alpha_2}{d_1} < K_1 < \frac{r_2 d_1}{r_2 + d_1} \text{ and } r_1 > r_2 > d_2.$$

$\bar{E}$ is local asymptotic stable if

$$\beta > \frac{d_1 K_1 K_2 r_2 + K_2 r_2 \alpha_2}{K_1(r_2 - d_2)} \text{ and } \alpha_1 < \frac{4 d_1 K_2 r_1 r_2}{{d_2}^2 - 2 d_2 r_2 + {r_2}^2}.$$

Proof. By using Schur-Cohn criterion, we obtain that $\bar{E}$ is locally asymptotically stable if and only if

$$\left|-1 - e^{-K_1 r_1 \bar{M}}\right| < 1 + e^{-K_1 r_1 \bar{M}} + \frac{\bar{N}\left(1 - e^{-K_1 r_1 \bar{M}}\right)(\beta^2 K_1 r_1 - K_2 r_2 \alpha_1 \alpha_2)}{K_1 r_1 K_2 r_2} < 2. \quad (13)$$

The inequality (13) can be written

(a) $\left|-1 - e^{-K_1 r_1 \bar{M}}\right| < 1 + e^{-K_1 r_1 \bar{M}} + \frac{\bar{N}\left(1 - e^{-K_1 r_1 \bar{M}}\right)\left(\beta^2 K_1 r_1 - K_2 r_2 \alpha_1 \alpha_2\right)}{K_1 r_1 K_2 r_2}$

and

(b) $1 + e^{-K_1 r_1 \bar{M}} + \frac{\bar{N}\left(1 - e^{-K_1 r_1 \bar{M}}\right)(\beta^2 K_1 r_1 - K_2 r_2 \alpha_1 \alpha_2)}{K_1 r_1 K_2 r_2} < 2.$

If we consider condition (7) and (8), it can be easily seen that (a) is always holds. From (b), we hold

$$\frac{\bar{N}\left(1 - e^{-K_1 r_1 \bar{M}}\right)(\beta^2 K_1 r_1 - K_2 r_2 \alpha_1 \alpha_2) + K_1 r_1 K_2 r_2 e^{-K_1 r_1 \bar{M}}}{K_1 r_1 K_2 r_2} < 1$$

which reveal

$$\beta > \frac{K_1 K_2 r_2 + d_1 K_1 K_2 + K_2 \alpha_2}{r_2 - d_2}.$$

Under the condition

$$K_1 < \frac{r_2 d_1}{r_2 + d_1}$$

we can write

$$\beta > \frac{d_1 K_1 K_2 r_2 + K_2 r_2 \alpha_2}{K_1(r_2 - d_2)} > \frac{K_1 K_2 r_2 + d_1 K_1 K_2 + K_2 \alpha_2}{r_2 - d_2}$$

This completes the proof.

Example 1. The parameter values which are taken from [11] as $r_1 = 0.18$, $r_2 = 0.1045$, $k_1 = 5\text{x}10^6$, $k_2 = 3\text{x}10^6$, $\beta = 4.32\text{x}10^{-8}$, $\alpha_2 = 3.422\text{x}10^{-9}$, $d_1 = d_2 = 0.0412$ and the determined value $\alpha_1 = 2.27721\text{x}10^{-7}$ provide the conditions of Theorem 1. It can be seen that under the conditions given in Theorem 1, the positive equilibrium point $\bar{E} = (9.99394\text{x}10^5, 6.32449\text{x}10^5, 1.03287\text{x}10^6)$ of system (6) is local asymptotic stable (see Figure 1a), where blue, red and black graphs represent M(n), N(n) and Z(n) population densities respectively.

Theorem 2. Let the conditions of Theorem 1 hold. Moreover, assume that $r_1 - \alpha_1 N(n) > 0$, $r_2 - \beta N(n) - d_2 > 0$, $\beta Z(n-1) - d_1 - \alpha_2 M(n) < 0$.

If

$$r_1K_1M(n) < r_1 - \alpha_1 N(n) < \ln\left(\frac{2\bar{M} - M(n)}{M(n)}\right),$$

$$r_2K_2Z(n) < r_2 - \beta N(n) - d_2 < \ln\left(\frac{2\bar{Z} - Z(n)}{Z(n)}\right),$$

and $M(n) < \bar{M}$, $N(n) > 2\bar{N}$, $Z(n) < \bar{Z}$ then the positive equilibrium point $\bar{E}$ is globally asymptotically stable.

Proof. Let

$$V(n) = [E(n) - \bar{E}]^2 \ , n = 0,1,2 \ldots$$

is a Lyapunov function with the positive equilibrium point $\bar{E} = (\bar{M}, \bar{N}, \bar{Z})$. The change along the solutions of the system is

$$\Delta V(n) = V(n+1) - V(n)$$
$$= \{E(n+1) - E(n)\}\{E(n+1) + E(n) - 2\bar{E}\}.$$

In addition, the change along the solutions of the first equation in system (6) is

$$\Delta V_1(n) = [M(n+1) - M(n)][M(n+1) + M(n) - 2\bar{M}].$$

It can be seen that if $r_1K_1M(n) < r_1 - \alpha_1 N(n)$, $A_1 < \ln\left(\frac{2\bar{M} - M(n)}{M(n)}\right)$ and $M(n) < \bar{M}$ then $\Delta V_1(n) < 0$. Similarly, it can be shown that $\Delta V_2(n) = [N(n+1) - N(n)][N(n+1) + N(n) - 2\bar{N}] < 0$ and $\Delta V_3(n) = [Z(n+1) - Z(n)][Z(n+1) + Z(n) - 2\bar{Z}] < 0$. As a result, we obtain $\Delta V(n) = (\Delta V_1(n), \Delta V_2(n), \Delta_3 V(n)) < 0$.

Example 2. In order to try the conditions of Theorem 2, initial conditions can be determined as $M(1) = 4x10^5$, $N(1) = 1x10^5$, $Z(1) = 1x10^5$ and parameter values can be taken Example 1. Figure 1b shows that under the conditions given in Theorem 2 the positive equilibrium point is global asymptotic stable, where blue, red and black graphs represent $M(n)$, $N(n)$ and $Z(n)$ population densities respectively.

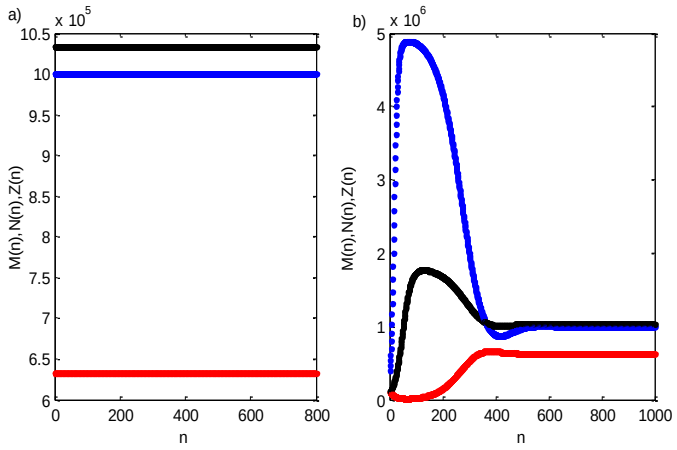

Figure 1. The iteration solution of $M(n)$, $N(n)$ and $Z(n)$ for different initial conditions.

3. Neimark-Sacker bifurcation analysis

In this section, we try to determine Neimark-Sacker bifurcation point of the system by using Schur-Cohn criterion that is given as follows.

Theorem A ([28])**.** A pair of complex conjugate roots of

$$p(\lambda) = \lambda^3 + p_2\lambda^2 + p_1\lambda + p_0 \qquad (14)$$

lie on the unit circle and the other roots of $p(\lambda)$ all lie inside the unit circle if and only if

(a) $p(1) = 1 + p_2 + p_1 + p_0 > 0$ and

$$p(-1) = 1 - p_2 + p_1 - p_0 > 0,$$

(b) $D_2^+ = 1 + p_1 - {p_0}^2 - p_0p_2 > 0,$

(c) $D_2^- = 1 - p_1 - {p_0}^2 + p_0p_2 = 0.$

If we rearranged the equation (10), characteristic equation can be obtained as the form (14) where

$$p_2 = -1 - e^{-K_1r_1\bar{M}} - e^{-K_2r_2\bar{Z}},$$

$$p_1 = e^{-K_1r_1\bar{M}} + e^{-K_2r_2\bar{Z}} + e^{-K_1r_1\bar{M} - K_2r_2\bar{Z}}$$
$$+ \frac{\beta^2}{K_2r_2}\bar{N}\left(1 - e^{-K_2r_2\bar{Z}}\right) - \frac{\alpha_1\alpha_2}{K_1r_1}\bar{N}\left(1 - e^{-K_1r_1\bar{M}}\right),$$

$$p_0 = -\frac{\beta^2}{K_2r_2}\bar{N}e^{-K_1r_1\bar{M}}\left(1 - e^{-K_2r_2\bar{Z}}\right) - e^{-K_1r_1\bar{M} - K_2r_2\bar{Z}}$$
$$+ \frac{\alpha_1\alpha_2}{K_1r_1}\bar{N}e^{-K_2r_2\bar{Z}}\left(1 - e^{-K_1r_1\bar{M}}\right).$$

By using these results, bifurcation point can be determined as the following example.

Example 3. Solving equation c of Theorem A, we get $\bar{\beta} = 2.94043x10^{-7}$. Moreover, we have also $p(1) = 0.000386701 > 0$, $p(-1) = 7.47232 > 0$ ve $D_2^+ = 0.488065 > 0$ for this point. Figure 2 shows that $\bar{\beta}$ is the Neimark-Sacker bifurcation point of the system with the eigenvalues $\lambda_1 = 0.869464$ and $|\lambda_{2,3}| = |0.998519 \pm 0.0544078i| = 1$ where blue, red and black graphs represent $M(n)$, $N(n)$ and $Z(n)$ population densities respectively.

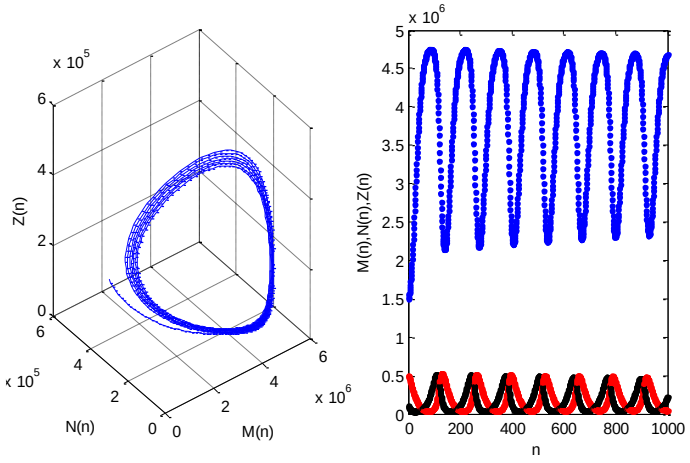

Figure 2. Neimark-Sacker bifurcation of system (6) for $\bar{\beta} = 2.94043x10^{-7}$, *where* $M(1) = 1.5x10^6$, $N(1) = 5x10^5$, $Z(1) = 1x10^5$. *The other parameters are taken Example 1.*

As seen in Figure 2, a stable limit cycle occurs at the bifurcation point $\bar{\beta}$ as a result of Neimark-Sacker bifurcation. This result leads to stable periodic solutions around the positive equilibrium point. Determining bifurcation point is very important issue for the control of the tumor cell population. After the bifurcation point, tumor and immune system will exhibit unstable oscillatory behavior, thus resulting uncontrolled tumor growth. The solutions of the system at the point $\beta = 1.14043x10^{-7} < \bar{\beta}$ can be seen in Figure 3, where the system has damped oscillation and the positive equilibrium point is local asymptotic stable. At the point $\beta = 4.34043x10^{-7} > \bar{\beta}$, system (6) has unstable oscillation and the positive equilibrium point is unstable (see Figure 4).

Finally, we can compare our theoretical results to the system (4) that is given in [11]. In study [11], a hopf bifurcation that is continuous case of Neimark-Sacker bifurcation is occurred around positive equilibrium point through stable limit cycle. Thus, we can say that bifurcation results of system (6) and system (4) are similar.

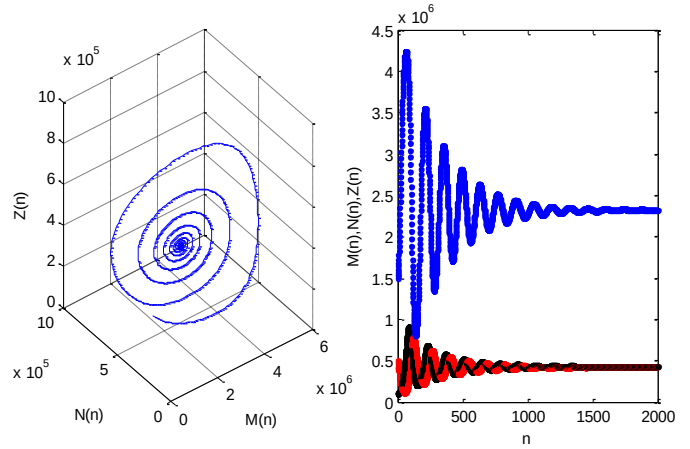

Figure 3. The iteration solution of the system for $\beta = 1.14043x10^{-7}$. *The other parameters and initial conditions are the same as Figure 2.*

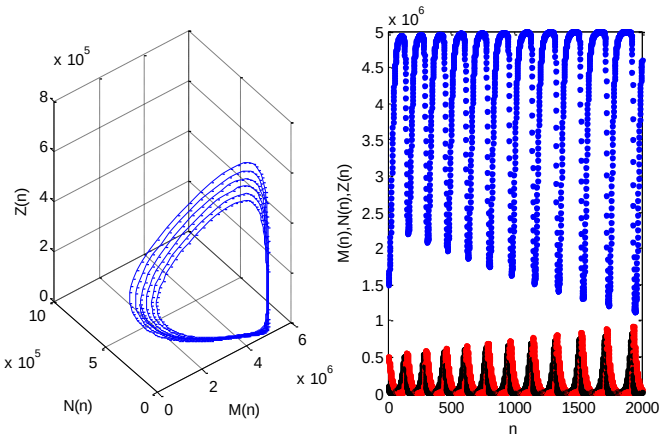

Figure 4. The iteration solution of the system for $4.34043x10^{-7}$. *The other parameters and initial conditions are the same as Figure 2.*

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The Investigation of Using For Gasoline Atomization of Ultrasonic Sound Generated By Piezoelectric Ceramic

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Abstract

Fuel atomization is important for internal combustion engine. Therefore in this study ultrasonic atomization method is used as a new atomization method. The ultrasonic sound generation using field and properties, especially by cavitations effect on liquids scanned in literature. Ultrasonic atomization method was compared with the existing experimental injector atomization data. Scaled droplets were occurred as a result of atomization. Image processing method was used for droplet size.

As a result experimental findings transformed into image and graphics. Pictures and graphics were interpreted and written to paper.

Keywords: Injector, ultrasonic atomization, cavitation, image processing method, droplet size.

1. Introduction

With all efforts to find new sources of energy, burning is, still, the main way to generate energy. This justifies the specialists studies focused on improving combustion systems. They must achieve a more complete combustion, a higher efficiency, and also have minimized pollutant emissions [1]. The atomization is very important to fuel combustion because it is effect on combustion efficiency. For this reason there are main methods of liquid fuel atomization.

One of them, which is using internal combustion engine, is mechanical spraying by pressure. In this method, a higher-pressure pump is needed because atomization is through higher-pressure. This is disadvantage.

One latter method, which is using ultrasonic nebulizer device, ultrasonic cleaner device and ultrasonic emulsion, is ultrasonic cavitation method. In this method, ultrasonic sound generated by piezoelectric ceramic that is the crystal salt. Ultrasonic cavitation is the formation of a gas bubble in the liquid during the rarefaction cycle. During the collapse tremendous pressures are produced. The pressure may be of the order of several thousand atmospheres. Thousands of these small bubbles are formed in a small volume of the liquid.

1.1. Ultrasonic Waves and Properties

A zone of compression and an adjacent zone of rarefaction constitute one cycle of an ultrasound wave. A wave cycle can be represented as a Fig.1 of local pressure (particle density) in the medium versus distance in the direction of the ultrasound wav. The distance covered by one cycle is the wavelength of the ultrasound wave. The number of cycles per unit time (cps, or just sec−1) introduced into the medium each second is referred to as the frequency of the wave, expressed in units of hertz, kilohertz, or megahertz where 1 Hz equals 1 cps. The maximum height of the wave cycle is the amplitude of the ultrasound wave.

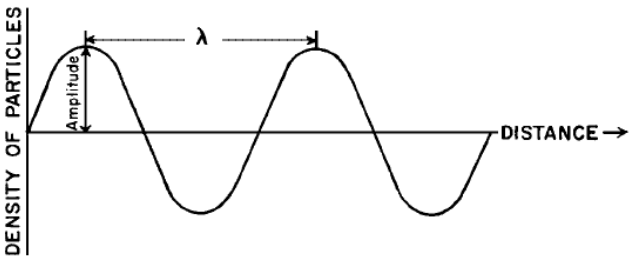

Figure.1 Characteristic of an Ultrasound Wave

Table 1. Table1. Frequency Classification of Ultrasound

Frequency (Hz)	Classification
20-20,000	Audible sound
20,000- 1,000,000	Ultrasound
1,000,000- 30,000,000	Diagnostic Medical Ultrasound

1.2. Velocity of Ultrasound

The velocity of spread sound depends on two importance parameter in medium. One of them is stiffness of the material constituent medium. The latter of them is density of the mass medium [2].

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Table 2. The spread velocity of sound in from the various substances

Substance	Density (gr/cm^3)	Velocity (m/sec)
Air	0,001	331
Oil	0,93	1450
Water	1,0	1540
Bone	1,85	4080
Aluminum	2,7	6400

1.3. Application Area of Ultrasound

The use of industry;

- To bring metals into thin powder
- To prepare emulsions of very fine-grained photo
- To make custom metal alloys
- To separate gases, gas mixtures
- To prevent contamination of the environment by cleaning air gases from factory chimneys
- Textile, metal coating, watchmaker, to make the cleaning process, such as requiring extreme cleanliness
- To make ultrasonic drilling machine for hard metals drilling and the processing
- Foundry, to purify molten metal from gases and to control crystal growth
- To use sonar device on submarine and ships

The use of medicine;
Ultrasound devices, which are commonly used in the medicine, are the most commonly used diagnostic's method [3].

1.4. Piezoelectric Effect

The electromechanical generators can be magnetostrictive or piezoelectric. The feeder of the piezoelectric generator converts electrical energy of 50/60Hz into electrical energy with high frequency. This energy is transmitted to the piezoelectric transducer which is converted into mechanical vibrations. When the electrical energy applied to upon piezoelectric material, the mechanical vibrations occur between the ends of crystal. At the same time the vibration creates the wave of ultrasound wave. Through the propagation of this wave, compression and rebound action occur, where the pressure is positive, negative, respectively. In areas with negative pressure, vapor bubbles can be formed. Cavitation phenomenon is produced due to intense local pressure because of cavities extinction and implosions. This occurs during compression, when positive pressure annihilate cavity. During cavities implosion, particularly those near the liquid surface are generated by intense hydraulic shocks. These shocks initiate disintegration of liquid film and production of droplets.

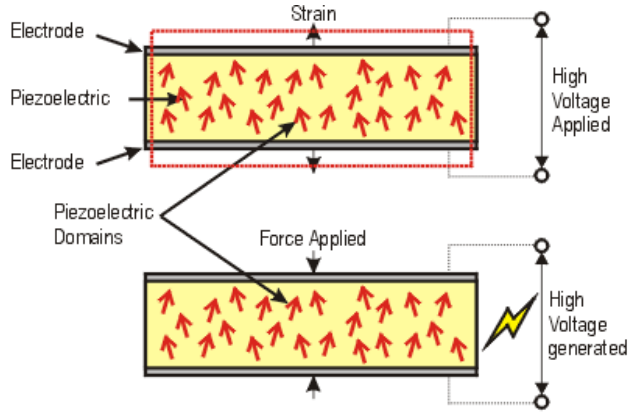


Figure 2. Piezoelectric Effect

1.5. Ultrasonic Nebulization

In the ultrasonic nebulizer used to create vapor are used piezoelectric crystal which is made vibration higher than 1 MHz's. Crystal transducer is made from materials such as quartz-barium, titanium, converts electrical signal to sound. Bunch of sound, which is focused in the liquid, generates waves. When the frequency and amplitude is strong enough, wave crest, which is like umbrella, reaches surface of liquid. The ultrasonic sound spread in the liquid is given an energy and act to the molecules of liquid. So it begins rupture the surface of liquid and liquid is converted the fog.

Figure.3 Ultrasonic sound effect on a water droplet

2. Material and methods

In this study of used method is experimental study. The experiment mechanism was founded for ultrasonic atomization. At the same time a camera system was founded for measurement droplet size. During operation, the finding of experiment was transmitted in the computer. Image taken from was analyzed the image processing program. On the other hand, a conventional injector which is used internal combustion engine that it is called MPI injection system was investigated under the similar conditionals.

This comparison was made for to see between differences of atomization methods.

2.1. Experimental Mechanism

Pro The main purpose of this experiment is to compare the droplet size generated by ultrasonic sound and conventional gasoline injector. vide sufficient detail to allow the work to be reproduced. Methods already published should be indicated by a reference: only relevant modifications should be described.

2.1.1. Gasoline Direct Injection System

In this experiment was compared gasoline direct injection system because in the spark ignition engine latest injection technology is this technology. It is more efficient than other gasoline injection systems. Atomization is better. Therefore, gasoline direct injection system that it is in the literature was compared with ultrasonic atomization.

At the article, was made by L. Alloca and et al. in 2009, they were prepared as follows an experiment mechanism.

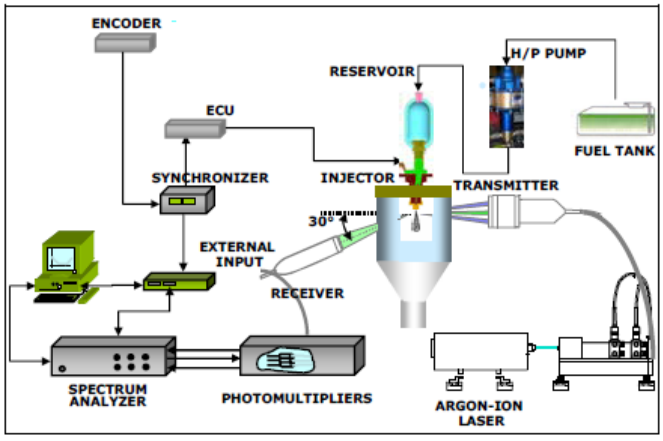


Figure.4 The experiment Mechanism set up by L. Alloca and et al.[4].

As a result of this study, at the gasoline direct injection system was occurred droplet size as following shows graphic.

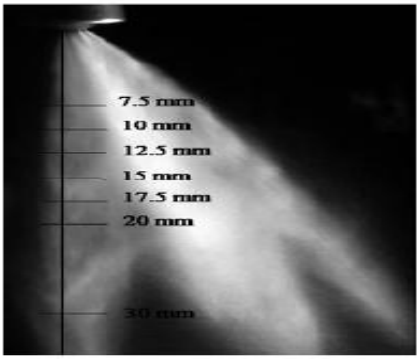


Figure.5 Measurement grid

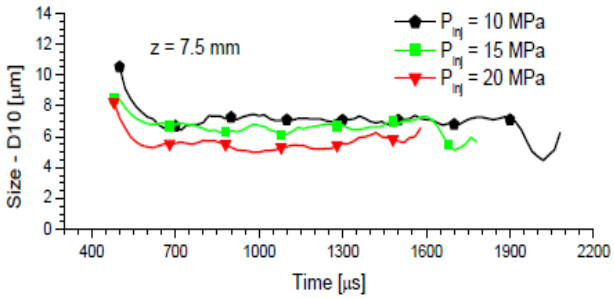


Figure 6 The investigated points have been 7.5mm from the nozzle

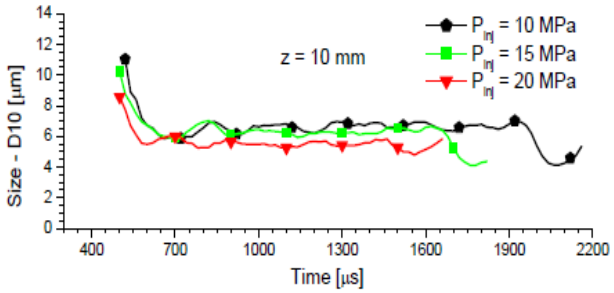
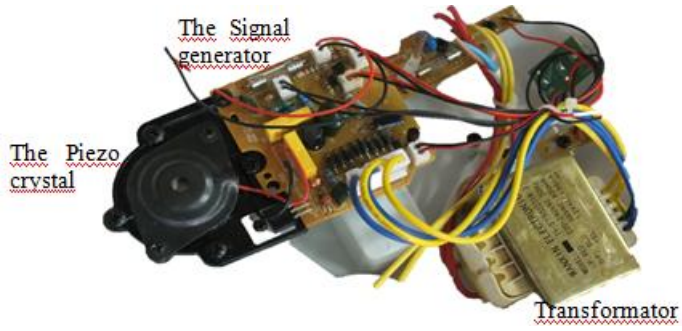


Figure 7 The investigated points have been 10mm from the nozzle

Shows the above graphs changed between 6 to 12µm of droplet size at the gasoline direct injection.

2.1.2. The Ultrasonic Atomization System

In this system the most important advantage is no need the pressure. So without pressure is made the better atomization. Schematic view of the experiment mechanism of ultrasonic atomization as follows.



Figur8 The experimental mechanism of ultrasonic generator.

In this mechanism, the electric voltage reduced from 220V to 12-40V by the transformator . The signal generator is produces the necessary signal for contraction and relaxation of piezo crystal. When this signals goes on piezo crystal, ultrasonic sound is produced. That the ultrasonic sound wave sent on the liquid, it is begun atomization.

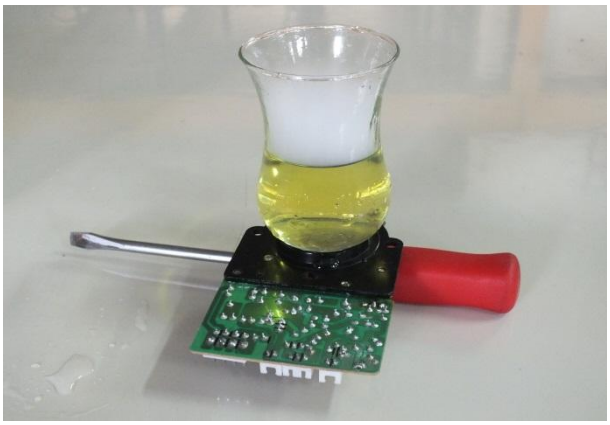


Figure 9 Gasoline and particle of gazoline

After ultrasonic atomization process, the occuring droplets were saved by the a microscobis camera (Dino-Lite USB camra).

Figure 10 Dino-Lite USB Camera which was used experiment.

The camera is established on of the atomization area. when the droplets come stagnant standstill, the image was saved.

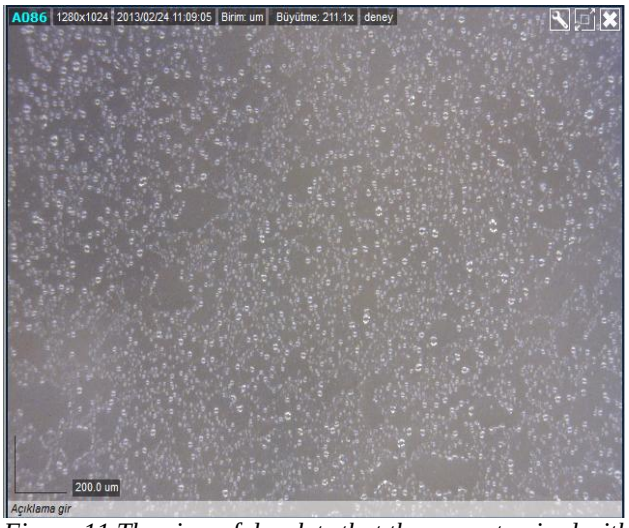


Figure 11 The view of droplets that they are atomized with ultrasonic sound.

This image is enlarged image of 211.1 times of micron dimensional droplets by microscobic camera. Also, it was enlarged 2 times at the computer.

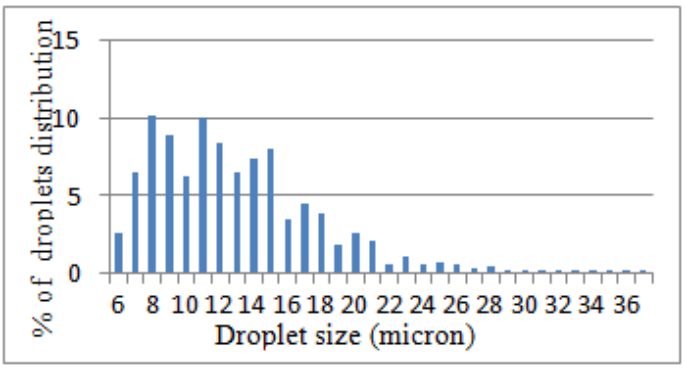


Figure 12 Ultrasonic droplet radius size

In this graph, droplet sizes which crumbles with the ultrasonic atomization method, is observed. Although Droplet radius size is change between 6 to 36 micron, 7 to 15 micron droplets is more than. So, there is a heterogeneous distribution. This condition is desired to increase combustion efficiency.

3. Results and Discussion

In this study was compared ultrasonic atomization method and GDI injection method and was observed that without pressure also is possible to achieve micron size droplet. In the above-described study, similar droplet size of ultrasonic method to achieve was used 20 MPa pressure. So, in the GDI system using of the high pressure pump has disadvantage than ultrasonic system. Also, in the ultrasonic system, be changeable of droplet size by frequency is advantage this system. Percentage of droplet distribution is suitable for combustion phases. Therefore, the ultrasonic injection system increases combustion efficiency.

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Genotyping of human papillomavirus high-risk types and correlation with potential risk factors

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Abstract

Human papillomavirus (HPV) is one of the most common sexually transmitted disease (STD) worldwide. HPV is a small, double-stranded DNA virus that infects mucosal and coetaneous epithelia trough tiny cuts and abrasion, exposed by the cells of the basal layer. If diagnosed on time HPV can be successfully treated, however, in some cases it can lead to the development of tumor. Most of cervical tumors contain HPV DNA, and majority of them contain high-risk types HPV16 and HPV18. Different risk factors are associated with HPV infection, including behavioral and biological predispositions. Aim of this study is to genotype potentially infected patients on high-risk types HPV DNA and to correlate the results with patient's different biological and lifestyle factors. For this purpose 20 gynecological smear samples were collected from women, previously subjected to the survey. Methodology included DNA extraction and real-time polymerase chain reaction (RT-PCR). Results showed that out of 20 patients five were positive for high risk HPV. Four of five positive patients were positive on HPV16 type of which one had HPV16 together with others high risk types. One of five positive patients was positive on HPV18 type and other high risk types not identified. Final outcome indicates the correlation of potentially endangered patients with specific sexual behavior and lifestyles, and furthermore represent the general consensus and awareness level this disease has on the public.

Key Words: Human papillomavirus (HPV), HPV high risk types, RT-PCR

1. Introduction

Human papillomaviruses (HPVs) comprise a highly diverse group of small, non-enveloped double-stranded DNA viruses that belong to the Papillomaviridae family. They are agents of the most common sexually transmitted diseases that can infect both females and males. HPV infection is very common among men and women across all geographical, racial and socio-economic subgroup worldwide [1]. Probably the widespread of this infection, made HPV one of the most researched issue today. If diagnosed on the time this disease can be successfully treated, however in some cases it can progress to a cancer. Recent studies indicated that over 99% of cervical tumors contain HPV DNA, approximately 65% of them contain the most common high-risk types HPV 16 and 18. Using DNA sequence determination and classification, genotypes such as 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68 are classified as high-risk types, meaning that they are prone to develop a cancer [2]. The International Committee on the Taxonomy of Viruses (ICTV) has classified the papillomaviruses as a distinct taxonomy family, the *Papillomaviridae*. Taxonomy status of papillomavirus types is based on the sequence of L1 gene, which are different from each other by at least 10%, 2-10%, and maximally 2% [3]. In benign cervical lesions, viral DNA is maintained in a free, extra chromosomal circular form termed episome, but, in many cervical cancers the DNA is integrated into the host genome. It is also demonstrated that the integration occurs more frequently in carcinomas associated with

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HPV 18 than in those associated with HPV 16. Integrated HPV was detected in 72% of the HPV 16 associated carcinomas compared to 100% of the HPV 18 associated carcinomas. In some cases it is also possible that both the integrated HPV DNA and episomal HPV DNA coexist [4]. According to the information from Institute for Public Health FBH in 2009 year cervical cancer was third malignance of ten leading malignances among women suffering from cancer in Federation BiH. In the year 2009 out of 2715 women suffering from cancer, 215 is diagnosed with cervical cancer, in percentage 7,9% out of 2715 cases. In the year 2010, number of women suffering from cervical cancer decreased for 11.63% giving the nubmber of 190 cases. Risk factors for HPV infection can be of biological or behavioral nature. Biologically based risk factors primarily affect downstream transitions in the oncogenesis pathway rather than risk for acquiring HPV. They include HPV virus its self and intrinsic host factors affecting immune response. Known or proposed host factors include immunosupression and human immunodeficiency virus infection, cooccurrence of other sexually transmitted infections such as Chlamydia trachomatis, herpes simplex virus, micronutrient deficiency, genetic polymorphism in the human leukocyte antigen (HLA) system, and patient age. Different studies have demonstrated that younger individuals have increased risk for HPV infection. The highest prevalence of HPV occurs among adolescent and young adults between the age of 15 and 25, and it is estimated that more than 75% of new HPV infections occur in individuals of this age range. Behaviorally based risk factor primarily affects the acquisition of HPV infection. They include characteristics of women's sexual history (number of partners and contraceptive use) and substance use history (alcohol, cigarettes, illicit drugs). Taking in consideration sexual history characteristics, increased number of lifetime sexual partners and having had a recent new sexual partner are two factors that have been consistently shown to be associated with an increased risk of HPV infection. Impact of substances use on risk for HPV infection has been similarly difficult to assess. Some studies showed that current or past cigarette smoking can be associated with the acquisition of HPV infection, progression to precancerous lesions and cervical cancer, but most of other studies failed to support this connection. [5]

2. Objective

Aim of this study is to genotype potentially infected female patients on high-risk types HPV DNA and to correlate the results with patient's different biological and lifestyle factors. Final outcome should indicate the correlation of potentially endangered patients with specific sexual behavior and lifestyles, and furthermore represent the general consensus and awareness level this disease has on the public.

3. Materials and Methods

3.1 Patients. Twenty women being at risk for HPV infection were tested at Institute for Biomedical Diagnostics and Research "NALAZ". Only after their consent and patients agreement, tested samples were implemented in this study. Samples were collected from *cervic uteri* (cervix). For the collecion and transport of cervical specimens and detection of HPV, *Abbot Cevi-Collect Specimen Collection Kit (USA)* was used. Collection tubes are stored at 2˚- 8˚C before the DNA extraction, and at -20˚C after the DNA extraction.

3.2 DNA Extraction. To extract HPV DNA ABBOTT *mSample Preparation System$_{DNA}$ for RealTime High Risk HPV extraction kit (USA)* was used. The purpose of sample preparation is to extract, concentrate and purify the target DNA molecules for amplification. The process is based on magnetic particle use, that capture nucleic acids and washes the particles to remove unbound sample components. After the nucleic acids are eluted PCR amplification was preformed.

Real-Time PCR (*RealTime High Risk HPV, Abbott, USA)* amplifies and detects High Risk (HR) HPV DNA in cervical cells collected in liquid media. The detection of HR HPV genotypes is achieved through a primer mix targeting a conserved L1 region of HPV genome and single stranded DNA probes. The assay can differentiate between HPV 16, HPV 18 and non-HPV 16/18 genotypes. A primer mix consists of three forward and two reverse primers targeting a conserved L1 region of HPV genome (approx. 150bp). Signal for HR HPV genotypes is generated with the use of fluorescent labeled probe (*TaqMan probe*). Internal Control (IC) amplicons are generated with a primer set targeting an endogenous human β-globin sequence and are detected with the IC specific probe. Probes for HPV 16, HPV 18, non-HPV 16/18 genotypes and IC are labeled with different fluorophores allowing their signals to be distinguishable in a single reaction. In each of 96-wells, 25 µl of the amplification master mix is added, together with 25 µl of sample elute giving the total volume of 50 µl. 25 µl of the amplification master mix contains: 11,6 µl Activation Reagent, 16,8 µl HPV oligonucleotide reagent (primers) and 2,9 µl AmliTaq Gold Enzyme.

3.3 Results

In the period of three months (March-May, 2013), out of twenty tested women five were positive for HPV infection. Three patients (p1261, p1105, p1062) had HPV16 type. One patient (p1427) had HPV16 types and was co-infected with others HPVs that were not identified. One patient (p1066) had HPV18 type and others HPVs detected as well (Fig. 1). Important factors

such as sexual behavior and lifestyle were analyzed for HPV positive patients. Patients were questioned about other sexual transmitted diseases (STDs) and four of infected patients had *Candidiasis*, commonly known as fungal infection. One patient (p1105) was negative for other STDs. Age of first sexual intercourse for four positive patients was between fifteen and twenty (15-20) years old. One patient (the same that was negative for other STDs) had first sexual intercourse with older than twenty (>20) years old. Question about contraceptive use, was positive for all infected patients. Four patients had more than one sexual partner during their lifetime; one patient (p1261) had one sexual partner (Table 2). Alcohol and cigarette consumption can increase the risk for HPV infection. Out of five positive patients four of them were positive for cigarette consumption, one patient was negative (p1105) (Fig. 2). Answers for alcohol consumption were classified as Never, Rare (1-2 glass per month), Often (1-2 Glass per week) and Very often (1-2 glass per day). All of the HPV positive patients were positive for alcohol consumption of which four were Rare, and one (p1261) was Often (Fig. 3 and table 3).

Table 1: HPV genotyping results. Results of HPV testing was classified as HPV negative, HPV16 positive, HPV16 and other type positive, and HPV18 and other type positive.

Patient's Code	Year	Place	HPV
p1608	20-25	KS	Neg
p1487	25-30	KS	Neg
p1427	20-25	KS	**HPV16/others**
p1372	25-30	KS	Neg
p1356	20-25	KS	Neg
p1340	25-30	KS	Neg
p1294	25-30	KS	Neg
p1289	30-40	KS	Neg
p1263	30-40	KS	0neg
p1261	30-40	KS	**HPV16**
p1235	30-40	KS	Neg
p1163	30-40	KS	Neg
p1133	25-30	KS	Neg
p1105	25-30	KS	**HPV16**
p1104	30-40	KS	Neg
p1086	25-30	KS	Neg
p1080	>40	TK	Neg
p1066	20-25	KS	**HPV18/others**
p1064	25-30	KS	Neg
p1062	30-40	KS	**HPV16**

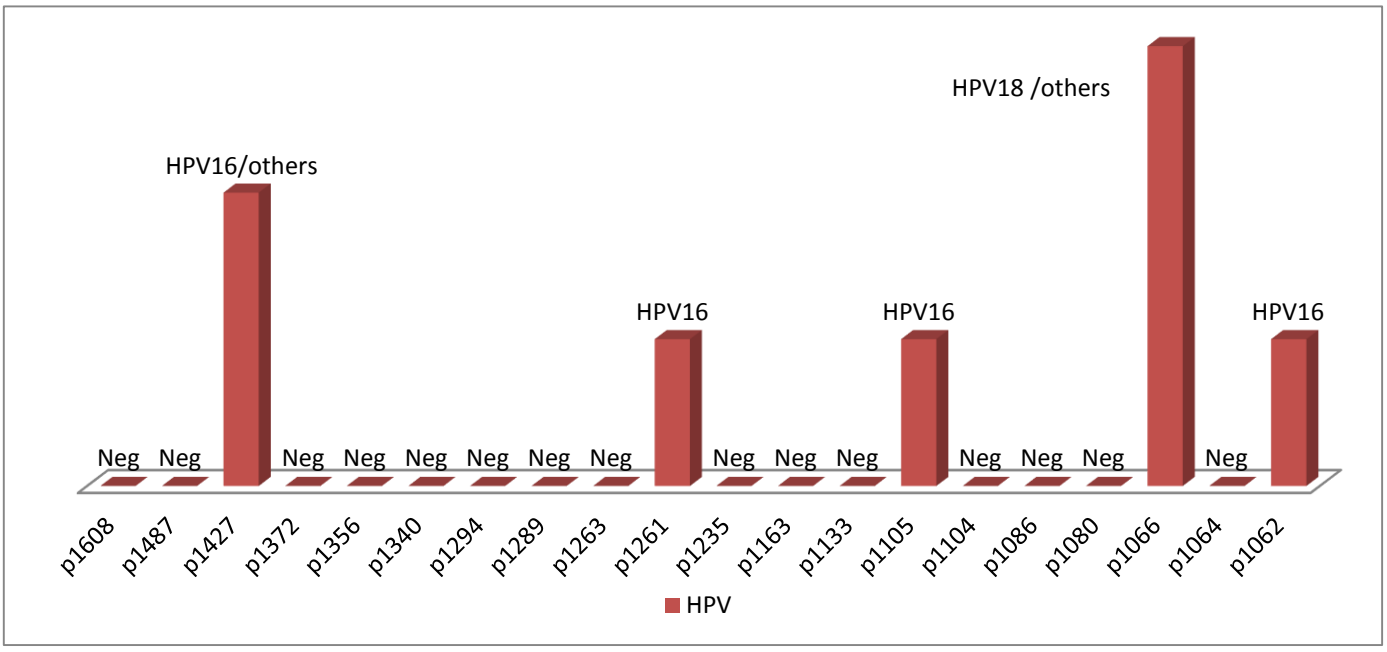

Figure 1: Schematic representation of HPV positive patients

Table 2: Correlation of HPV positive patients with the type of STDs and sexual behavior

Patient's Code	HPV type	Other STDs	1. sexual intercourse	Contraception	> 1 sexual partners
1427	HPV16/others	Candida	15-20	Condom and Pills	Yes
1261	HPV 16	Candida	15-20	Contracetive Pills	No
1105	HPV16	Neg.	>20	Condom	Yes
1066	HPV18/others	Candida	15-20	Condom	Yes
1062	HPV16	Candida	15-20	Condom and Pills	Yes

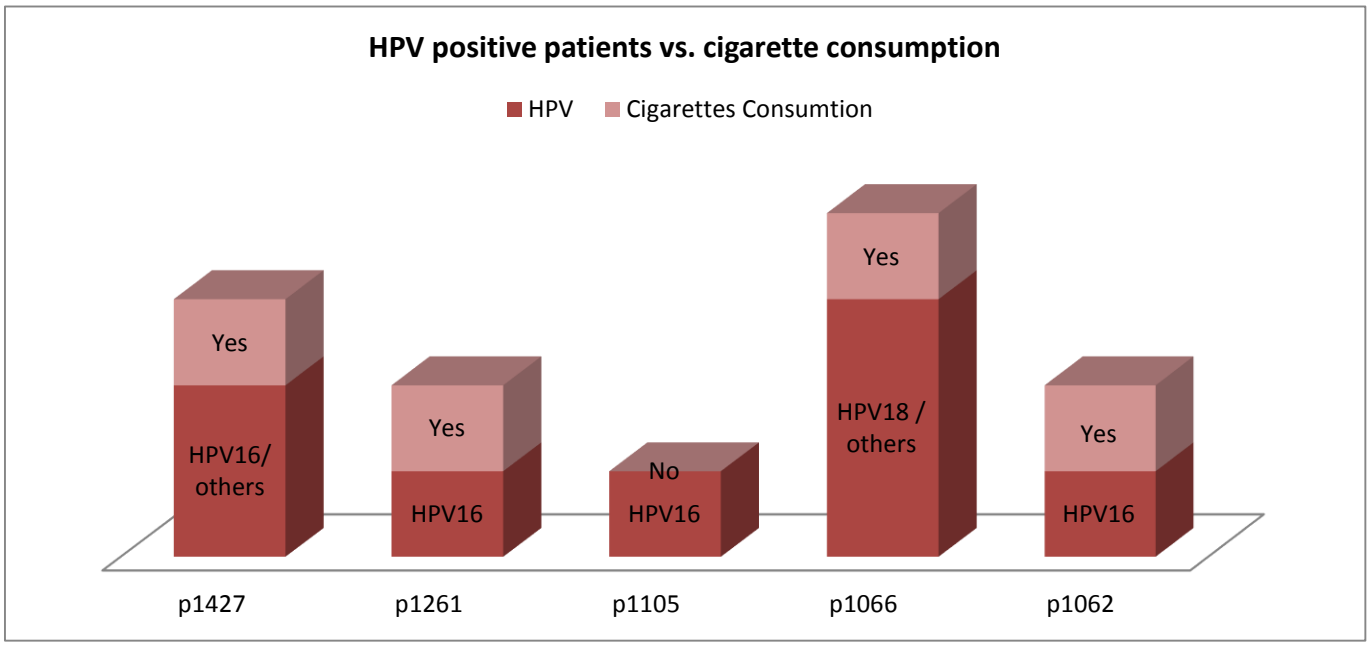

Figure 2: Schematic representation of HPV positive patients vs. cigarette consumption

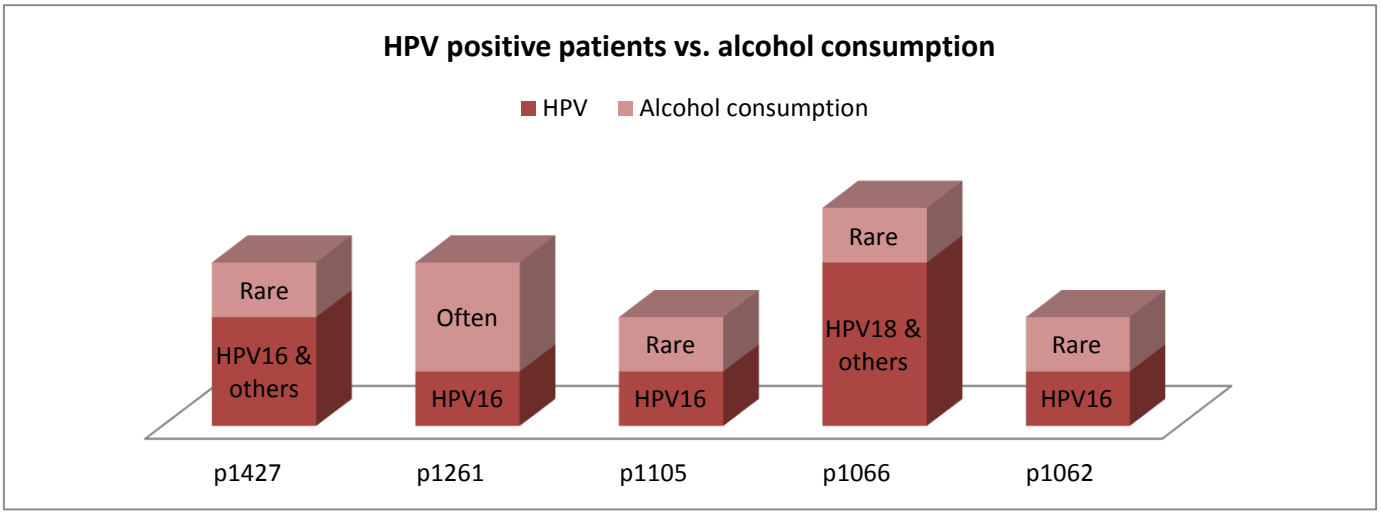

Figure 3: Schematic representation of HPV positive patients vs. alcohol consumption

To estimate the general consensus and awareness level that HPV infection has on the public, tested patients were subjected to the survey. Results are showing that the level of general information about HPV infection is relatively low (Fig. 4). Furthermore, only three of twenty patients knew about HPV HR types 16 and 18 (Fig. 5) and twelve patients never have heard about HPV vaccines existence, and three patients didn't know that HPV infection
can lead to cervical cancer development (Fig. 6 and 7). Only two patients get the idea to do HPV testing by themselves, while other eighteen patients were sent by their gynecologists (Fig. 9).

Table 3: Correlation of HPV positive patients with cigarettes and alcohol consumption

Patient's Code	HPV	Smoker	Alcohol use
1427	HPV16/others	Yes	Rare
1261	HPV16	Yes	Often
1105	HPV16	No	Rare
1066	HPV18/others	Yes	Rare
1062	HPV16	Yes	Rare

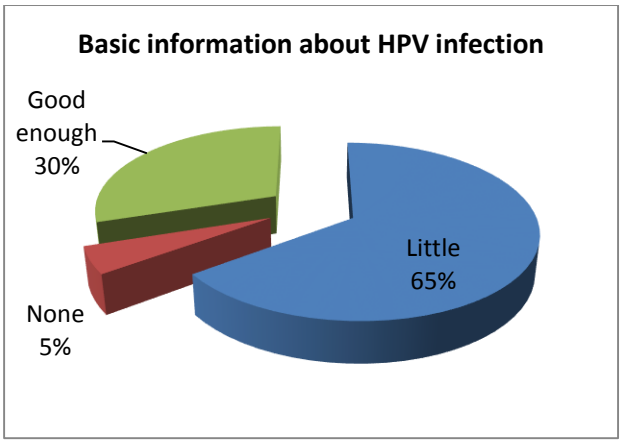

Figure 4: Basic information about HPV infection among twenty tested patients: good enough 30% (6patients), little 65% (13 patients) and none 5% (1patient).

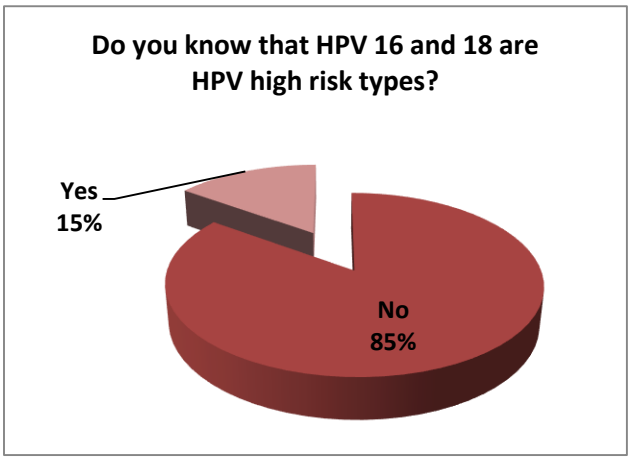

Figure 5: Knowledge about HPV high risk types: 15% (3 patients) knew about HPV HR 16 and 18 types, and 85% (17 patients) didn't know about HPV HR 16 and 18 types.

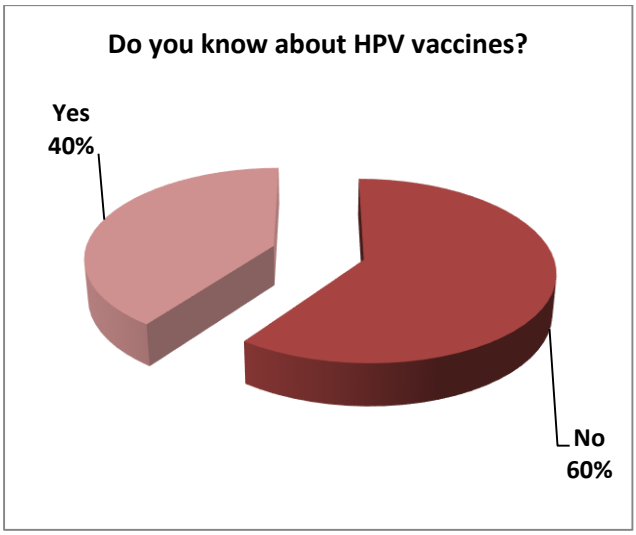

Figure 6: Awareness about HPV vaccines: 40% (8 patients) knew about HPV vaccines, 60% (12 patients) didn't know.

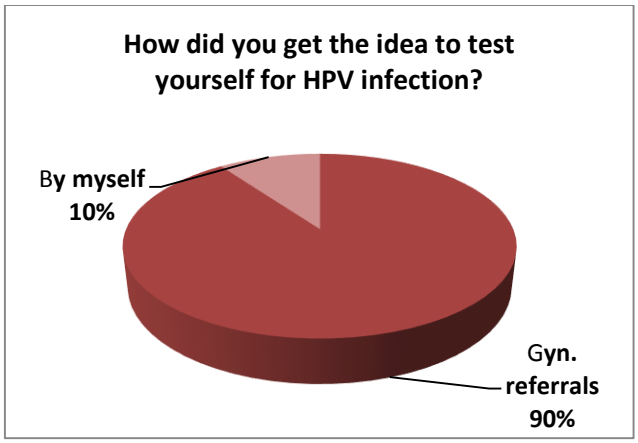

Figure 7: Patients referrals: Only 10% (2 patients) of patients get the idea to do HPV testing by themselves, while 90% (18 patients) of them get gynecological referrals.

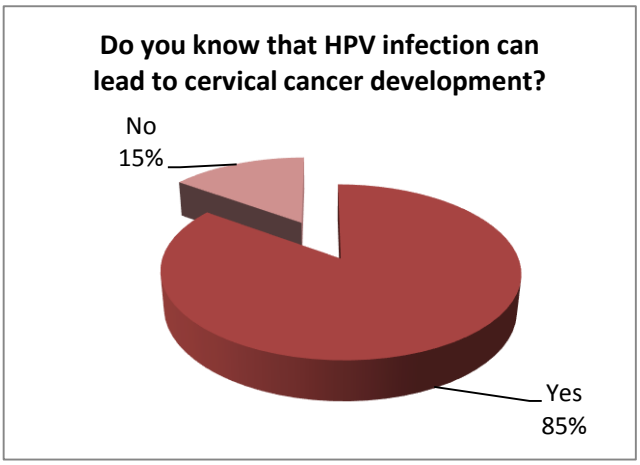

Figure 8: Knowledge about how the HPV infection is correlated with cancer: 15% (3 patients) didn't know that HPV infection can progress to cervical cancer, and 85% of them (17 patients) knew that fact.

4. Discussion

In the period of three months during which time this study was conducted, out of twenty patients, five of them were positive for HPV infection. The majority of positive results were identified as HPV HR 16 type. This proves the frequency of this particular HPV type among HPV infected patient. One patient was identified as HPV HR 18 type positive. Two of five infected patients were also co infected with other HR HPV types that were not identified. They had a combination with HR HPV other types and HPV HR 16 or HPV HR 18 type. All of the results suggest that HPV HR types, and especially HR HPV 16 and 18 are commonly found among HPV infected patients, leading to an increased risk for cervical cancer. As previously stated, over 99% of cervical tumors contain HR HPV DNA, and 65% of them contain HR types HPV 16 and 18. All of the infected patients were from Canton Sarajevo. The reason for this could be that people from rural areas are less informed about this type of infection. Age difference among the infected patients is pretty high (from 20 to 40 years old). Two of the infected patients were in the age

group from 20 to 25 years, one from 25 to 30, and the other two patients from 30 to 40 years old. HPV infection is present among the young as much as in middle aged individuals. Two younger patients in the range from 20 to 25 were co-infected with other HR HPV together with HPV16 or HPV18 HR type. A possible reason for this is that young individuals tend to change their sexual partners more frequently, or it can be caused by lack of adaptive immune response. Sexual behavior and other risk factors can increase predisposition for HPV infection. All of the HPV positive patients used contraception. Four positive patients used condom as contraception, while two of them use condom in combination with contraceptive pills. Only one patient used just contraceptive pills. Using condoms as contraception in most cases can protect us from getting this type of infection, however some level of risk exist. Only one positive patient used contraceptive pills that could increase the risk for infection. Pills can protect individuals from unwanted pregnancy, but they can't prevent the infection with sexually transmitted disease (STD).

Becoming sexually active at early age and multiple numbers of lifetime sexual partners are important risk factors. Age range of first sexual intercourse for four of infected patients was between 15 to 20 years old. Only one patient was more than twenty years old. Year range between 15 to 20 years can't be estimated as to early period for becoming sexually active, taking in consideration that most of individuals become sexually active with eighteen or nineteen years old. What is important here to mention is that individuals that became sexually active earlier have higher predisposition for HPV infection. This was indicated also with our data, since four out of five infected patients became sexually active in the period from 15 to 20 years old, while only one patient was over twenty years old. Four of five positive patients had more than one sexual partner during their lifetimes, and only one positive patient had one sexual partner. Again our data is supporting the fact that increased number of sexual partners, increase predisposition for HPV infection. The risk factors also increases with recent change of sexual partner, but this information was not included in our survey. Being co-infected with other STDs, primarily affects downstream transition in the oncogenesis pathway, rather than risk for acquiring HPV. Four HPV positive patients had Candidiasis or fungal infection in their lifetime. *C. albicans* is the most prevalent species in the majority of cases of asymptomatic colonization and vulvovaginal candidiasis. Certain species of Candida are more pathogenic than others, and they can induce hyphal and pseudohyphal formation, and enhance proteolytic activity and antigen modulation. These properties enable Candida to penetrate the mucosal surface and induce mucosal swelling, erythema, and exfoliation of cells. Individuals with abnormal vaginal microbiota, can have higher risk for formation of cervical cytologic abnormalities than woman without these conditions [6]. Behavioral risk factors such as alcohol consumption and cigarette smoking can be also associated with higher risk for HPV infection. Our results are showing that all five infected patients were positive for alcohol use, and four of them were positive for cigarette smoking. General information about HPV infection was obtained by the patient's survey answers. Most of the patients (65%) were poorly informed about this infection. Only one patient wasn't informed at all. We can estimate that overall knowledge about HPV is relatively poor. Positive fact is that most of the patients knew that HPV infection can lead to cervical cancer development. Keeping this in mind one should reconsider the level of seriousness that this infection can bring. Only three patients knew about HR HPV types. Considering our environment and educational system this can be caused by lack of readily found information's about HPV infection. Situation about HPV vaccines information wasn't as bad as expected, since HPV vaccines are relatively new approach in medicine.

Eight tested patients knew about HPV vaccines existence. Low awareness level about this infection is also estimated, by the information that of all twenty patients only two of them got the idea to do HPV test by themselves, while other eighteen were sent by their gynecologists. This proves us that people from this area are not concerned about their sexual health. Since we don't have any sexual education in our elementary or high schools, many people are not concerned because they don't know that this disease even exists.

5. Conclusion

HPV is one of the most common sexually transmitted disease in the world. Variations that exist among HPV viruses, make this disease harder to treat. Its silent infection and evasion can cause this disease to proliferate without any signs or symptoms, eventually leading to cervical cancer development. Because of this it is important to know the seriosity that this infection can bring. If it is estimated that 90% of cervical tumors contain HR HPV DNA, than public awareness and regular testing on HPV infection could drastically decrease the risk for cervical cancer. Solution for HPV infection in the future can be in HPV vaccines. Since people from our country still don't have the accessibility to this type of vaccination; increasing the awareness level through our education system about STD can be the alternative solution. If people are not informed about STD, and if they don't know what are the risk factors, they can't protect themselves from this type of disease. Awareness about HPV infection will not only decrease the level of infected patient, but will also decrease the number of patients suffering from cervical cancer.

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AN INTEGRATED APPROACH USING DEMATEL, ANP AND TOPSIS FOR EVALUATING RESEARCH & DEVELOPMENT PROJECTS

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Abstract

Research and development (R&D) projects should be one of the main dimensions of universities for providing academic development. It is also a core performance indicator for monitoring and ranking universities. For these reasons, usually there are many projects submitted to the institutions that fund R&D projects. Funding institutions should evaluate the submitted projects in terms of multi-criteria and select the suitable ones among them. Therefore multi-criteria decision making techniques can be implemented as a useful tool for these kinds of problems. In this study an integrated approach which includes DEMATEL, ANP and TOPSIS methods is used for evaluating and ranking projects. The criteria are determined by taking the Turkish Scientific and Technical Research Institute's (TÜBİTAK) project selection procedures into consideration. DEMATEL method is used in order to detect the cause and effect interaction among main criteria. Then ANP method is implemented for calculating the weights of each criterion. Finally, TOPSIS method is applied for ranking the projects.

Keywords: Project Selection, Multi-criteria Decision Making, DEMATEL, ANP, TOPSIS.

1. Introduction

Research and development (R&D) projects should be one of the main dimensions of universities for providing academic development. Having R&D projects increases the quality of universities. It is also a core performance indicator for monitoring and ranking universities. Moreover, universities' long-term strategy of increasing R&D projects generates economic value for its country and the community. For these reasons, usually there are many projects submitted to the institutions that fund R&D projects. Funding institutions should evaluate the submitted projects in terms of multi-criteria and select the suitable ones among them.

Evaluation is an essential tool that not only helps measuring projects' success, but also contributes to their success. Evaluation helps managers to plan, verify, and communicate what they aim to do, to decide how to allocate resources, to learn how best to modify or redesign programs and to estimate the project outputs, outcomes, and impacts (Ruegg, 2007). The main purpose while considering R&D-projects is to ensure that they are evaluated effectively, and to select ones which achieve the maximized benefit.

Meade and Presley (2002) revealed three major themes for R&D project selection: (1) The need to relate selection criteria to corporate strategies. (2) The need to consider qualitative benefits and risks of candidate projects. (3) The need to reconcile and integrate the needs and desires of different stakeholders. Besides, the need of group decision making methods can arise in addition to these items. Because, R&D project selection involves multiple interrelated criteria and qualitative factors that are difficult to be measured by an individual expert. Similarly, limitations of existing R&D project selection identified by Chien (2002) are:

- inadequate treatment of multiple, often interrelated, evaluation criteria;
- inadequate treatment of project interrelationships among projects;
- inability to handle non-monetary aspects; e.g. diversity among projects
- no explicit recognition and incorporation of the experience and knowledge of R&D managers (i.e. the decision makers);
- perceptions by R&D managers that the models are difficult to understand and use.

Hence, the multi-criteria decision making techniques can be implemented as a useful tool for these kinds of problems.

Habib *et al.* (2009) present a method for R&D project selection that allows for the consideration of important interactions among decision levels and criteria. The methodology uses the ANP for this evaluation. The research paper concludes with a case study describing the

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implementation of this model at a small high-tech company, including data based on the actual use of the decision making model. The case study helps to verify that ANP is an effective and efficient decision-making tool. Similarly, Büyüközkan and Öztürkcan (2010) use ANP and DEMATEL technique to help companies determine critical Six Sigma projects and identify the priority of these projects especially in logistics companies.

Feng *et al.* (2011) present an integrated decision method for collaborative R&D projects that are applied by innovative research teams so called CIRT project. In this method, a hierarchy structure for CIRT project selection is constructed. The criteria for competitiveness and collaboration are finalized in light of literature review as well as real situations. Their study integrates analytic hierarchy process (AHP), scoring method and weighted geometric averaging method. Some sample data from the National Natural Science Foundation of China (NSFC) is used to illustrate the potential application of the proposed method.

This study aims to propose an evaluation approach based on a combined DEMATEL, ANP and TOPSIS methods in order to select R&D projects. In this study, the criteria are determined by taking the Turkish Scientific and Technical Research Institute's (TÜBİTAK) project selection procedures into consideration. DEMATEL method is used in order to detect the cause and effect interaction among main criteria. Then ANP method is implemented for calculating the weights of each criterion. Finally, TOPSIS method is applied for ranking the projects.

The structure of the rest of the paper is: In the next section, the evaluation framework is introduced and the techniques are explained. Then, implementation of the proposed integrated decision making method is detailed. Finally, some conclusions and discussions are given in the last section.

2. Evaluation framework

As indicated before, the project evaluation and selection procedures of TÜBİTAK is investigated, and four main criteria and 15 sub-criteria are determined. These criteria are given in Table 1.

Table 1. Project evaluation and selection criteria

C1: Originality
C11: Innovation of technology
C12: Scientific part of the project
C13: Improvement on research capability
C2: Quality of the Methodology
C21: Relevance of the techniques
C22: Opportunity of success
C23: Convenience of the literature
C24: Risk Management
C3: Feasibility
C31: Quality of work program
C32: Relevance of infrastructure
C33: Capability of research team
C34: Relevance of the budget
C4: Impact
C41: Economic benefit
C42: Social benefit
C43: Technological extendibility
C44: Dissemination plan

The study proposes an integrated approach in which DEMATEL, ANP and TOPSIS methods are used in a combined manner. The following three subsections clarify these methods.

The DEMATEL Methodology

DEMATEL method was developed by Gabus and Fontela (1972). It analyzes the influential status and strength between the factors and converts them into an explicit structural mode of a system (Lin and Wu, 2008).

The steps of DEMATEL technique are explained below;

Step 1: Generating the direct-relation matrix: An evaluation scale of 0, 1, 2, 3, and 4 is used for influential comparison where 0 represents "no influence" while 4 represents "very high influence". A group of experts is asked to make pairwise comparisons between criteria. To compound all opinions from *K* experts, the direct-relation matrix *A* is calculated using Eq. (1) by averaging each expert's scores.

$$a_{ij} = \frac{1}{K}\sum_{k=1}^{K} x_{ij}^{k} \qquad (1)$$

where the x_{ij}^{k} is the score given by the k^{th} expert indicating the influential level that factor *i* has on factor *j*.

Step 2: Normalizing the direct-relation matrix: The normalized direct-relation matrix *M* can be obtained by normalizing *A* using Eqs. (2) and (3).

$$M = k.A \qquad (2)$$

$$k = Min\left(\frac{1}{\max\limits_{1\le i\le n}\sum_{j=1}^{n} a_{ij}}, \frac{1}{\max\limits_{1\le j\le n}\sum_{i=1}^{n} a_{ij}}\right) \qquad (3)$$

Step 3: Obtaining the total-relation matrix: The total-relation matrix *T* can be obtained by using Eq. (4), where *I* denotes the identity matrix.

$$\mathrm{T} = \mathrm{M} + \mathrm{M}^2 + \mathrm{M}^3 + \ \ldots = \sum_{\mathrm{i}=1}^{\infty} \mathrm{M}^{\mathrm{i}} = \mathrm{M}(\mathrm{I} - \mathrm{M})^{-1} \qquad (4)$$

where $T = \left[t_{ij}\right]_{n\times n}, i, j = 1, 2, \ldots, n.$

Step 4: Compute the dispatcher group and receiver group: The vectors *D* and *R* represent the sum of rows and columns of matrix *T* respectively (Eqs. 5 and 6). *D* + *R* value indicates the degree of importance that the corresponding criterion plays in the entire system. The factor having greater value of *D* + *R* has more interrelationships with other factors. On the other hand, criteria having positive values of *D* – *R* are on the cause group and dispatches effects to the other criteria. On the contrary, criteria having negative values of *D* – *R* are on the effect group and receive effects from the other criteria.

$$D = \sum_{j=1}^{n} t_{ij} \qquad (5)$$

$$R = \sum_{i=1}^{n} t_{ij} \qquad (6)$$

Step 5: Set up a threshold value to obtain the causal diagram: Since the total-relation matrix *T* provides the information on how one criterion affects another, decision maker group should set up a threshold value in order to filter out some negligible relationships.

The ANP Methodology

ANP is the general form of analytic hierarchy process (AHP) and was proposed by Saaty (1996) to overcome the problem of interrelation among criteria or factors. It provides measurements to derive ratio scale priorities for the distribution of influence between factors and groups of factors in the decision (Saaty, 2001). The feedback structure does not have the top to bottom form of a hierarchy but looks more like a network, with cycles connecting its components of elements, which we can no longer call levels, and with loops that connect a component to itself (Saaty, 2005).

Through a supermatrix, whose entries are themselves matrices of column priorities, the ANP synthesizes the outcome of dependence and feedback within and between clusters of elements (Yang and Chang, 2012). The initial supermatrix must be transformed to a matrix in which each of its columns sums to unity. For this reason, this matrix must be normalized by the cluster's weight to get the column sums to unity. Hence, the weighted supermatrix is obtained (Saaty and Vargas, 1998). The supermatrix representation is given in Fig. 1.

$$W = \begin{array}{c} \\ C_1 \\ C_2 \\ \vdots \\ C_m \end{array} \begin{array}{c} \begin{array}{cccc} C_1 & C_2 & \cdots & C_m \\ e_{11} \dots e_{1n_1} & e_{21} \dots e_{2n_2} & \cdots & e_{m1} \dots e_{mn_m} \end{array} \\ \begin{pmatrix} W_{11} & W_{12} & \cdots & W_{1m} \\ W_{21} & W_{22} & \cdots & W_{2m} \\ \vdots & \vdots & \ddots & \vdots \\ W_{m1} & W_{m2} & \cdots & W_{mm} \end{pmatrix} \end{array}$$

Figure 1. The supermatrix representation

Pairwise comparisons between the criteria can be implemented according to dependency relationships which are obtained from DEMATEL approach in order to generate local weights assessing relative importance value using a scale of 1 (equal importance) to 9 (extreme importance).

The TOPSIS Methodology

The technique for order preference by similarity to an ideal solution (TOPSIS) was proposed by Hwang and Yoon (1981) and expanded by Chen and Hwang (1992). The main principle in TOPSIS method is that, in a graph, any chosen alternative should have the shortest distance from the ideal solution and the farthest distance from the negative-ideal solution (Opricovic and Tzeng, 2004).

The TOPSIS technique is implemented using the following steps (Triantaphyllou, 2000; Opricovic and Tzeng, 2004):

Step 1. Calculate the normalized decision matrix: D is the decision matrix which refers to *n* alternatives that are evaluated in terms of *m* criteria.

$$D = \begin{bmatrix} x_{11} & \cdots & x_{1n} \\ \vdots & \ddots & \vdots \\ x_{m1} & \cdots & x_{mn} \end{bmatrix}$$

R is the normalized decision matrix and r_{ij} is an element of *R*. The normalized value r_{ij} is calculated as:

$$r_{ij} = \frac{x_{ij}}{\sqrt{\sum_{j=1}^{m} {x_{ij}}^2}}, \quad i = 1, \dots, m; \quad j = 1, \dots, n \quad (7)$$

Then the *R* matrix is formed as follows:

$$R = \begin{bmatrix} r_{11} & \cdots & r_{1n} \\ \vdots & \ddots & \vdots \\ r_{m1} & \cdots & r_{mn} \end{bmatrix}$$

Step 2. Calculate the weighted normalized decision matrix: V is the weighted normalized decision matrix and v_{ij} is an element of *V*. The weighted normalized value v_{ij} is calculated as:

$$v_{ij} = w_i r_{ij}, \quad i = 1, \dots, m; \quad j = 1, \dots, n \quad (8)$$

where w_i is the weight of the *i*th criterion and $\sum_{i=1}^{m} w_i = 1$. Then the *V* matrix is formed as follows:

$$V = \begin{bmatrix} v_{11} & \cdots & v_{1n} \\ \vdots & \ddots & \vdots \\ v_{m1} & \cdots & v_{mn} \end{bmatrix}$$

Step 3. Determine the positive-ideal and the negative-ideal solutions: The positive-ideal donated as A^* and the negative-ideal donated as A^- alternatives are defined as:

$$A^* = \{v_1^*, \dots, v_m^*\} = \left\{\left(\max_j v_{ij} | i \in I'\right), \left(\min_j v_{ij} | i \in I''\right)\right\} \quad (9)$$

$$A^- = \{v_1^-, \dots, v_m^-\} = \left\{\left(\min_j v_{ij} | i \in I'\right), \left(\max_j v_{ij} | i \in I''\right)\right\} \quad (10)$$

where I' is associated with benefit criteria, and I'' is associated with cost criteria.

A^* indicates the most preferable solution and similarly A^- indicates the least preferable solution.

Step 4. Calculate the separation measure: The separation of each alternative from the positive-ideal solution and negative-ideal solution are calculated using *n*-dimensional Euclidean distance method. The distances from the positive-ideal solution and negative-ideal solution can be calculated as follows:

$$D_j^* = \sqrt{\sum_{i=1}^{m} \left(v_{ij} - v_i^*\right)^2}, \quad j = 1, \dots, n, \quad (11)$$

$$D_j^- = \sqrt{\sum_{i=1}^{m} \left(v_{ij} - v_i^-\right)^2}, \quad j = 1, \dots, n. \quad (12)$$

Step 5. Calculate the relative closeness to the ideal solution: The relative closeness of alternative A_j with respect to A^* is calculated as follows:

$$C_j^* = D_j^- / \left(D_j^* + D_j^-\right), \qquad j = 1, \ldots, n \tag{13}$$

where $0 \leq C_j^* \leq 1$.

If $A_j = A^*$ then C_j^* is equal to 1 and if $A_j = A^-$ then C_j^* is equal to 0.

Step 6. Rank the preference order: The best alternative can be now decided according to the preference rank order of C_j^*. Therefore, the best alternative is the one that has the shortest distance to the ideal solution.

3. Case study: R&D projects evaluation and selection

First of all, interactions among the main criteria are obtained by asking some academic experts using DEMATEL approach. As an example the evaluation of one of the experts is given in Table 2. Similarly, evaluations of the rest of the experts are obtained and then averages of numbers are calculated using Eq. (1) in order to form initial direct-relation matrix (see Table 3).

Table 2. The influential evaluation of an expert

	C1	C2	C3	C4
C1	0	1	3	4
C2	1	0	4	3
C3	1	2	0	3
C4	1	2	1	0

Table 3. The initial direct-relation matrix

	C1	C2	C3	C4
C1	0	1.5	2.25	3.5
C2	1.75	0	3.5	2.75
C3	1.25	1.75	0	2.5
C4	1.25	2	1.75	0

The normalized direct-relation matrix is obtained using Eqs. (2 and 3). After calculating the normalized direct-relation matrix, the total-relation matrix is obtained using Eqs. (4, 5, and 6). The total-relation matrix is shown in Table 4. The threshold value is determined as 0.55 by the experts. The values above the threshold are indicated in bold that give the cause and effect relationship among the main criteria. Those indicators are used in constructing pairwise comparison matrixes for ANP. For example C1 effects C2, as can be seen from Table 4, thus, pairwise comparison matrixes for sub-criteria of C2 are built for each sub-criterion of C1. As an illustrating example Table 5 gives the pairwise comparison matrix for one of the experts for sub-criteria of C2 in terms of criterion C11.

After taking the rest of the experts' evaluations, geometric average is calculated and then local weights are gained by following ANP approach (see Table 6).

Table 4. The total-relation matrix

	C1	C2	C3	C4
C1	0.38	**0.62**	**0.79**	**0.97**
C2	**0.58**	0.51	**0.95**	**0.98**
C3	0.43	**0.55**	0.48	**0.77**
C4	0.41	0.54	**0.63**	0.52

Threshold value = 0.55

Table 5. Pairwise comparison matrix of an expert for sub-criteria C2 in terms of criterion C11

	C21	C22	C23	C24
C21	1	1/5	3	3
C22	5	1	5	5
C23	1/3	1/5	1	3
C24	1/3	1/5	1/3	1

Table 6. Combined pairwise comparison matrix and the weights for sub-criteria C2 in terms of criterion C11

	C21	C22	C23	C24	Wi
C21	1	1.97	5.01	3.71	0.50
C22	0.51	1	3.31	2.34	0.28
C23	0.2	0.3	1	0.93	0.10
C24	0.27	0.43	1.07	1	0.12

Consistency value: 0.01

Similarly, the rest of the local weights are calculated based on the interactions obtained from the DEMATEL. Then, the unweighted supermatrix is formed for sub-criteria by placing the calculated local weights into the matrix in the proper places (see Table 7). Then, unweighted supermatrix is normalized to transform it to the weighted supermatrix in which each of its columns sums to 1. The power of the weighted supermatrix is taken until the values of each column are stabilized. These calculations are implemented using MATLAB software and the limit supermatrix is obtained which is given in Table 8. Any column of the matrix shows the weights of corresponding sub-criteria.

As a next step TOPSIS method is implemented after obtaining the local weights of each sub-criterion trough the limit supermatrix. TOPSIS method is used to score and rank the projects in terms of local weights and decision matrix which is built by scoring each project considering each criterion. The decision matrix is given in Table 9. Then, Table 9 is normalized by using Eq. (7) and multiplied by the weights obtained from ANP limit supermatrix, by using Eq. (8). The new table is called as the weighted normalized decision matrix. Then, the positive-ideal A^* and the negative-ideal A^- values are calculated by using Eqs. (9 and 10). Table 10 illustrates the weighted normalized decision matrix, and the values A^* and A^-.

The separation or distances of each alternative from the positive-ideal solution and negative-ideal solution are calculated using Eq. (11 and 12). Then, the relative closeness of alternative A_j is calculated using Eq. (13). Table 11 shows the overall results and the rank of each project.

As can be seen from Table 11, project 11 is found out as the best project because of having the greatest value of C^*. The amount of the projects to be selected for funding can be determined depending on the allocated budget. Table 11 would be useful while considering project election.

Table 7. The unweighted supermatrix

	C11	C12	C13	C21	C22	C23	C24	C31	C32	C33	C34	C41	C42	C43	C44
C11	0	0	0	0.23	0.41	0.11	0.30	0	0	0	0	0	0	0	0
C12	0	0	0	0.51	0.32	0.58	0.27	0	0	0	0	0	0	0	0
C13	0	0	0	0.26	0.27	0.31	0.43	0	0	0	0	0	0	0	0
C21	0.50	0.53	0.47	0	0	0	0	0.45	0.47	0.20	0.29	0	0	0	0
C22	0.28	0.11	0.10	0	0	0	0	0.16	0.22	0.41	0.36	0	0	0	0
C23	0.10	0.25	0.35	0	0	0	0	0.22	0.10	0.14	0.10	0	0	0	0
C24	0.12	0.11	0.08	0	0	0	0	0.16	0.21	0.25	0.25	0	0	0	0
C31	0.09	0.12	0.11	0.23	0.16	0.27	0.27	0	0	0	0	0.15	0.17	0.13	0.30
C32	0.17	0.25	0.26	0.38	0.23	0.31	0.22	0	0	0	0	0.25	0.20	0.28	0.27
C33	0.55	0.57	0.52	0.27	0.49	0.30	0.38	0	0	0	0	0.52	0.52	0.43	0.21
C34	0.19	0.06	0.11	0.12	0.12	0.12	0.14	0	0	0	0	0.08	0.11	0.16	0.22
C41	0.33	0.17	0.26	0.22	0.40	0.18	0.20	0.21	0.17	0.31	0.46	0	0	0	0
C42	0.17	0.11	0.07	0.10	0.20	0.13	0.10	0.10	0.10	0.11	0.09	0	0	0	0
C43	0.41	0.56	0.47	0.48	0.32	0.53	0.38	0.23	0.52	0.36	0.32	0	0	0	0
C44	0.10	0.17	0.20	0.20	0.08	0.16	0.31	0.46	0.21	0.22	0.14	0	0	0	0

Table 8. The limit supermatrix

	C11	C12	C13	C21	C22	C23	C24	C31	C32	C33	C34	C41	C42	C43	C44
C11	0.021	0.021	0.021	0.021	0.021	0.021	0.021	0.021	0.021	0.021	0.021	0.021	0.021	0.021	0.021
C12	0.031	0.031	0.031	0.031	0.031	0.031	0.031	0.031	0.031	0.031	0.031	0.031	0.031	0.031	0.031
C13	0.023	0.023	0.023	0.023	0.023	0.023	0.023	0.023	0.023	0.023	0.023	0.023	0.023	0.023	0.023
C21	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078
C22	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065
C23	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.034
C24	0.048	0.048	0.048	0.048	0.048	0.048	0.048	0.048	0.048	0.048	0.048	0.048	0.048	0.048	0.048
C31	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073
C32	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105
C33	0.165	0.165	0.165	0.165	0.165	0.165	0.165	0.165	0.165	0.165	0.165	0.165	0.165	0.165	0.165
C34	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056
C41	0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.081
C42	0.033	0.033	0.033	0.033	0.033	0.033	0.033	0.033	0.033	0.033	0.033	0.033	0.033	0.033	0.033
C43	0.118	0.118	0.118	0.118	0.118	0.118	0.118	0.118	0.118	0.118	0.118	0.118	0.118	0.118	0.118
C44	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067

Table 9. Decision matrix for the projects

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19	P20
C11	60	40	45	75	50	65	70	30	55	75	90	60	60	55	85	80	70	75	45	40
C12	55	35	50	75	50	70	75	40	50	70	85	50	65	50	75	75	75	65	50	45
C13	30	45	45	60	60	65	60	35	50	60	75	55	45	45	60	55	65	50	40	35
C21	65	45	50	70	55	70	75	40	60	75	90	65	60	55	80	80	75	70	50	45
C22	70	50	50	75	60	70	75	45	65	75	95	60	65	60	80	85	75	75	50	50
C23	60	40	55	75	55	75	75	40	55	75	85	55	70	55	75	75	70	70	55	50
C24	40	50	55	60	65	50	45	35	40	55	75	70	70	75	65	50	43	57	65	52
C31	55	55	57	63	60	75	58	42	42	50	70	70	75	65	65	60	55	60	65	55
C32	65	65	60	73	55	80	75	55	45	65	80	75	75	60	60	65	60	70	75	70
C33	55	40	45	75	80	70	65	50	55	55	85	80	80	75	70	75	75	65	65	60
C34	75	75	70	80	80	85	85	70	70	75	80	75	65	70	70	80	85	80	75	65
C41	85	80	60	60	85	80	70	65	65	60	70	70	60	75	70	75	80	80	75	75
C42	65	70	75	80	80	55	50	50	55	65	75	55	60	70	70	75	75	65	60	55
C43	55	55	60	55	65	60	50	50	55	60	80	65	65	70	75	75	70	55	50	45
C44	60	60	65	70	70	75	60	50	50	60	65	75	70	60	65	70	45	45	50	60

Table 10. The weighted normalized decision matrix, and positive and negative ideal solutions

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19	P20	A^*	A^-
C11	.004	.003	.003	.006	.004	.005	.005	.002	.004	.006	.007	.004	.004	.004	.006	.006	.005	.006	.003	.003	.007	.002
C12	.006	.004	.006	.008	.006	.008	.008	.004	.006	.008	.010	.006	.007	.006	.008	.008	.008	.007	.006	.005	.010	.004
C13	.003	.004	.004	.006	.006	.006	.006	.003	.005	.006	.007	.005	.004	.004	.006	.005	.006	.005	.004	.003	.007	.003
C21	.017	.012	.013	.019	.015	.019	.020	.011	.016	.020	.024	.017	.016	.015	.022	.022	.020	.019	.013	.012	.024	.011
C22	.015	.011	.011	.016	.013	.015	.016	.010	.014	.016	.020	.013	.014	.013	.017	.018	.016	.016	.011	.011	.020	.010
C23	.007	.005	.006	.009	.006	.009	.009	.005	.006	.009	.010	.006	.008	.006	.009	.009	.008	.008	.006	.006	.010	.005
C24	.007	.009	.010	.011	.012	.009	.008	.007	.007	.010	.014	.013	.013	.014	.012	.009	.008	.011	.012	.010	.014	.007
C31	.015	.015	.015	.017	.016	.020	.016	.011	.011	.014	.019	.019	.020	.018	.018	.016	.015	.016	.018	.015	.020	.011
C32	.023	.023	.021	.026	.019	.028	.026	.019	.016	.023	.028	.026	.026	.021	.021	.023	.021	.025	.026	.025	.028	.016
C33	.030	.022	.025	.041	.044	.039	.036	.028	.030	.030	.047	.044	.044	.041	.039	.041	.041	.036	.036	.033	.047	.022
C34	.012	.012	.012	.013	.013	.014	.014	.012	.012	.012	.013	.012	.011	.012	.012	.013	.014	.013	.012	.011	.014	.011
C41	.021	.020	.015	.015	.021	.020	.017	.016	.016	.015	.017	.017	.015	.019	.017	.019	.020	.020	.019	.019	.021	.015
C42	.007	.008	.008	.009	.009	.006	.006	.006	.006	.007	.008	.006	.007	.008	.008	.008	.008	.007	.007	.006	.009	.006
C43	.024	.024	.026	.024	.028	.026	.022	.022	.024	.026	.034	.028	.028	.030	.032	.032	.030	.024	.022	.019	.034	.019
C44	.015	.015	.016	.017	.017	.018	.015	.012	.012	.015	.016	.018	.017	.015	.016	.017	.011	.011	.012	.015	.018	.011

Table 11. Final performance indices of the projects

Rank	Projects	D^*	D^-	C^*
1	P11	0.0048	0.0393	0.8918
2	P16	0.0113	0.0305	0.7290
3	P15	0.0135	0.0284	0.6775
4	P12	0.0148	0.0301	0.6707
5	P13	0.0154	0.0302	0.6616
6	P6	0.0155	0.0281	0.6443
7	P17	0.0162	0.0275	0.6301
8	P4	0.0163	0.0276	0.6285
9	P5	0.0183	0.0276	0.6023
10	P14	0.0179	0.0261	0.5928
11	P7	0.0206	0.0233	0.5308
12	P18	0.0200	0.0225	0.5296
13	P10	0.0231	0.0195	0.4571
14	P19	0.0248	0.0203	0.4503
15	P1	0.0250	0.0172	0.4079
16	P20	0.0287	0.0160	0.3579
17	P9	0.0298	0.0123	0.2930
18	P3	0.0309	0.0126	0.2889
19	P2	0.0339	0.0118	0.2587
20	P8	0.0349	0.0072	0.1708

4. Conclusion

This paper proposes an approach for evaluating and selecting suitable R&D projects to be funded by an institution, based on hybrid multi-criteria decision making methods. The proposed approach also depends on group decision making concept. Turkish Scientific and Technical Research Institute's (TÜBİTAK) project selection procedures are taken into consideration for determining main and sub-criteria. In order to obtain cause and effect interaction among main criteria which will be required for ANP method, DEMATEL approach is implemented to the main criteria. Based on those cause and effect interrelationships, the weights of each sub-criterion are calculated by applying ANP methodology. Finally projects are evaluated and ranked using TOPSIS method. The projects having the highest performance indicator values can be selected according to the institute's financial budget. The proposed approach is justified by applying to a case study. This approach can also be implemented to other similar multi-criteria and group decision making problems.

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