

Optimizing Performance of Tablet's Direct Compression Process Using Fuzzy Goal Programming

Abbas Al-Refaie

Abstract—This paper aims at improving the performance of the tableting process using statistical quality control and fuzzy goal programming. The tableting process was studied. Statistical control tools were used to characterize the existing process for three critical responses including the averages of a tablet's weight, hardness, and thickness. At initial process factor settings, the estimated process capability index values for the tablet's averages of weight, hardness, and thickness were 0.58, 3.36, and 0.88, respectively. The L_9 array was utilized to provide experimentation design. Fuzzy goal programming was then employed to find the combination of optimal factor settings. Optimization results showed that the process capability index values for a tablet's averages of weight, hardness, and thickness were improved to 1.03, 4.42, and 1.42, respectively. Such improvements resulted in significant savings in quality and production costs.

Keyword—Fuzzy goal programming, control charts, process capability, tablet optimization.

I. INTRODUCTION

THE pharmaceutical industry is a vital segment of the health care system, which is regulated heavily as any mistakes in product design or production can be severe, costly and even fatal. The compressed tablet is the most popular dosage form in use today. Dolocet is a combination drug, an effective analgesic and antipyretic with a mild effect on the stomach. It is provided in tablet form. The Dolocet solid-dosage tablets are manufactured by compressing a powder formulation into a die. This processing technique is known as direct compression. It offers simplicity, economy, and the potential for high-volume output.

Typically, the tablet quality can be described by several quality characteristics including: (i) average weight; the dosage form of a drug is traditionally composed of two ingredients: the active pharmaceutical ingredient (API) which is the drug itself and is a measure of the effectiveness of a drug and the excipient, which is the substance of the tablet or the liquid the API is suspended in. API is used to measure the effectiveness of a drug. The upper and lower specification limits of the tablet weight are 617.4 mg and 642.6 mg. It is preferred that the average tablet weight at nominal, Nominal-The-Best (NTB) type response, (ii) average hardness in units of Kilopond (Kp). An acceptable hardness is required and tablet strength testing is necessary for both, research and development of new formulations and for quality control. The lower specification limit for the tablet hardness is 6 Kilopond

(Kp), which is considered the larger-the-better (LTB) type response, and (iii) Average thickness, which is important for packaging; the uniformity of the thickness indicates that the tablet press is performing well. Variation in the thickness will affect the tablets weight and hardness. The upper and lower specification limits of the tablet thickness are 3.99 mg and 4.41 mg, respectively; hence, the average tablet thickness is considered the nominal-the-best (NTB) type response [1].

The robust design proposed by Taguchi has been only found efficient for optimizing a single response of main interest [2]-[4]. Several approaches have been proposed to optimize process performance with multiple responses [5]-[7]. Nevertheless, determining precise targets for multiple quality responses is often a difficult activity for a process/product engineer [8]-[10]. Therefore, several formulations of goal programming (GP) models were introduced for solving the fuzzy GP (FGP) problems taking into account the decision-maker's (DM's) preferences [11]-[14]. An effective FGP technique is the weighted additive model, which considers all shapes of membership functions, with the objective to minimize the weighted deviations from the imprecise fuzzy values for all quality responses and process factors [15]-[19]. FGP has been utilized for optimizing process performance in many business applications [20]-[21].

In reality, determining the combination of optimal factor settings for tablet manufacturing processes to improve multiple quality responses is a real challenge. This paper, therefore, aims at optimizing the performance of direct compression process for multiple quality characteristics using statistical techniques and weighted additive model in fuzzy goal programming.

II. PROCESS PERFORMANCE AT INITIAL FACTOR SETTINGS

A. Control Charts

A control chart is one of the primary monitoring techniques of Statistical Process Control (SPC). Control charts plot the averages of measurements of quality characteristic in samples taken from the process versus the sample number. The chart has a center line (CL) as well as upper and lower control limits (UCL and LCL, respectively). At initial factor settings, the $\bar{x}-s$ charts for averages a tablet's weight, hardness, and thickness are shown in Fig. 1.

Obviously, the control charts indicate that the process is in statistical control for the three quality responses.

A. Al-Refaie is with the Department of Industrial Engineering in the University of Jordan, Amman, 11942 (e-mail: abbas.alrefai@ju.edu.jo).

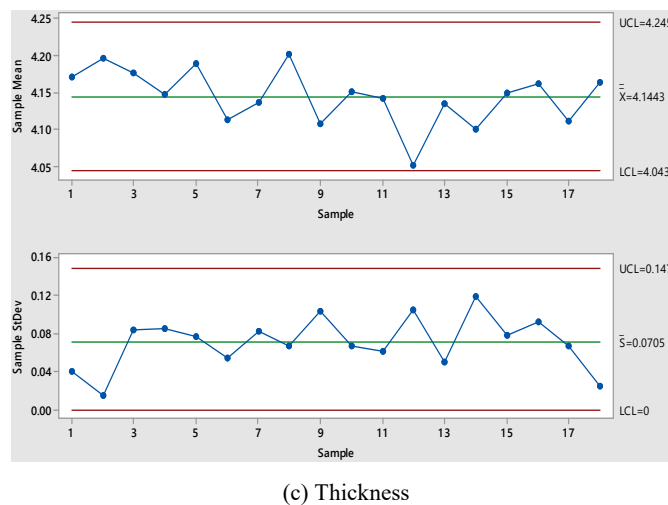
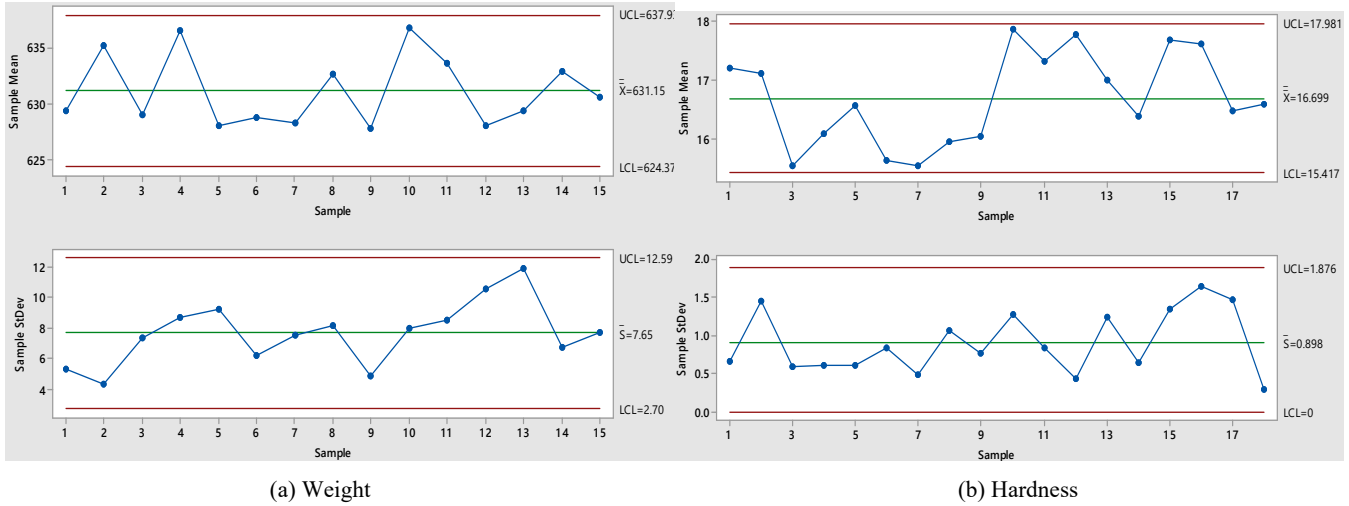


Fig. 1 The \bar{x} -s charts for average tablet at initial factor settings

B. Process Capability Analysis

Capability analysis is used to assess whether a process is statistically capable to meet a set of customer desired product specifications. In practice, the process standard deviation, σ , is unknown and is frequently estimated by:

$$\hat{\sigma} = \frac{\bar{s}}{c_4} \tag{1}$$

where c_4 is a constant related to the sample size, while \bar{s} is the CL value in the s chart. The actual process capability index (C_{pk}) attempts to take the target, T , into account. The C_{pk} estimator, \hat{C}_{pk} , can be expressed mathematically by:

$$\hat{C}_{pk} = \min \left\{ \frac{\hat{\mu} - LSL}{3\hat{\sigma}}, \frac{USL - \hat{\mu}}{3\hat{\sigma}} \right\} \tag{2}$$

where \bar{x} is the process mean estimated by the CL value of \bar{x} chart. Further, the multivariate process capability (MC_{pk}) is a

criterion for selecting an optimal design is known as MC_{pk} and is used as a capability measure for a process having multiple performance measures. MC_{pk} is a proposed system capability index for the process which is the geometric mean of performance measure of C_{pk} values.

$$MC_{pk} = \left(\prod_1^m C_{pk} \right)^{1/m} \tag{3}$$

where m is the number of quality characteristics. For the tablet's weight, 15 samples were taken; each of size 12. While, for each of the tablet's hardness and thickness, 18 samples were taken; each of size 10. The estimated UCLs and LCLs of the \bar{x} charts for average tablet weight, hardness, and thickness are displayed in Table I. The estimated means, standard deviations, and \hat{C}_{pk} values calculated and are listed in Table II.

In Table I, the \hat{C}_{pk} values are 0.58, 3.62 and 0.88 for the

Averages of tablet's weight, hardness, and thickness, respectively. As a result, the tableting process is capable regarding the average tablet hardness, because this value larger than the accepted level (1.33). However, it is found incapable for the averages of weight and thickness. Moreover, the calculated $\hat{M}_{C_{pk}}$ value (= 0.333) is less than one. These results indicate that further process improvement is needed.

III. PROCESS OPTIMIZATION

Three main process factors are identified affecting the tablet quality, including: Feed Speed (x_1); the speed where the feeder delivers powder from the hopper to the die table. Head Pressure (x_2); which is the amount of force that is applied to compress the powder into tablets. Finally, the Turret Speed (x_3), which is the rotational speed of the die punch. The three factors are assigned each at three levels. The current settings for the tablet dosage are: Feed Speed = 23 rpm, Pressure = 15 KN, and the Turret Speed = 13 rpm. The L_9 array shown in Table III is selected for experimental design. Twenty samples are selected; each of size 10, 5 and 5 are taken for the weight, hardness and thickness, respectively. Each experiment is repeated three times. The averages of averages are calculated for the three responses and recorded in Table III. Let $y_1, y_2,$

and y_3 denote the measured averages of weight, hardness, and thickness, respectively. To optimize process performance, the weighted additive model in fuzzy goal programming was utilized. The optimization procedure is described as follows: **Step 1:** Formulate the mathematical relationship between each quality response and process factors.

The regression model for the average tablet weight (y_1) is formulated as follows ($R^2_{adjusted} = 98.4$):

$$y_1 = 827 + 311.9x_1 - 324.6x_2 - 197.4x_3 - 6.84x_1^2 + 13.36x_2^2 + 11.1x_3^2 - 6.182x_2x_3$$

The regression model for y_2 is expressed as: ($R^2_{adjusted} = 84$):

$$y_2 = 194 + 64.8x_1 - 60.6x_2 - 60.3x_3 - 1.6x_1^2 + 1.2x_2^2 + 2.32x_3^2 + 1.06x_2x_3$$

Finally, the regression model for y_3 is expressed as: ($R^2_{adjusted} = 87.4$):

$$y_3 = 2.87 + 0.18x_1 + 1.54x_2 - 1.83x_3 - 0.073x_1x_2 - 0.07x_1x_3 - 0.012x_2x_3$$

TABLE I
 ESTIMATED CONTROL LIMITS AND PROCESS CAPABILITY INDICES

Response	LSL	T	USL	Process settings	LCL	CL	UCL	LCL	CL	UCL	\hat{C}_{pk}
Weight	617.4	630	642.6	Initial	624.3	631.14	637.93	2.7	7.65	12.59	0.58
	617.4		642.6	Optimal	628.5	632.29	635.74	1.08	3.81	6.54	1.03
Hardness	6	16	*	Initial	15.43	16.71	17.98	0	0.90	1.88	3.62
	6		*	Optimal	15.78	17.09	18.39	0	0.91	1.90	4.45
Thickness	3.99	4.2	4.41	Initial	4.05	4.15	4.25	0	0.07	0.14	0.88
	3.99		4.41	Optimal	4.10	4.16	4.23	0	0.04	0.09	1.42

TABLE II
 PROCESS CAPABILITY AT INITIAL SETTINGS

Quality characteristic	Mean	Standard deviation	\hat{C}_{pk}
Average weight (mg)	631.15	8.19	0.58
Average hardness (Kp)	16.70	0.07	3.62
Average thickness (mm)	4.14	1.18	0.88

TABLE III
 EXPERIMENTAL DATA

	x_1	x_2	x_3	y_1	y_2	y_3
1	22	12	14	4.286	18.70	643.370
2	22	13	15	4.228	13.64	619.727
3	22	14	16	4.218	16.40	632.620
4	23	13	14	4.236	17.62	641.980
5	23	14	15	4.172	18.26	632.600
6	23	12	16	4.284	18.96	632.350
7	24	14	14	4.286	17.20	647.360
8	24	12	15	4.192	17.36	628.020
9	24	13	16	4.160	16.82	623.190

Step 2: Choose the suitable membership function representing each response. That is:

a) For the average tablet weight, which is of NTB type

response, the trapezoidal membership function, μ_{y_1} , is represented by:

$$\mu_{y_1} = \begin{cases} 0 & y_1 \leq 617.4 \\ 1 - \frac{630 - y_1}{12.6} & 617.4 \leq y_1 \leq 630 \\ 1 - \frac{y_1 - 630}{12.6} & 630 \leq y_1 \leq 642.6 \\ 0 & y_1 \geq 642.6 \end{cases}$$

Let $\omega_{y_1}^-$ and $\omega_{y_1}^+$ denote the negative and positive deviation from the weight target, then the corresponding constrains are:

$$\begin{aligned} y_1 + \omega_{y_1}^- - \omega_{y_1}^+ &= 630 \\ \mu_{y_1} + \frac{\omega_{y_1}^-}{12.6} + \frac{\omega_{y_1}^+}{12.6} &= 1 \\ \omega_{y_1}^-, \omega_{y_1}^+ &\leq 12.6 \end{aligned}$$

b) For the average tablet hardness, which is the LTB type,

the membership function, μ_{y_2} , is defined by:

$$\mu_{y_2} = \begin{cases} 0 & y_2 \leq 6 \\ 1 - \frac{17-y_2}{11} & 6 \leq y_2 \leq 17 \\ 0 & y_2 \geq 17 \end{cases}$$

Let $\omega_{y_2}^-$ denote the negative deviation, the y_2 goal constraints are written as:

$$\begin{aligned} y_2 + \omega_{y_2}^- &= 17 \\ \mu_{y_2} + \frac{\omega_{y_2}^-}{11} &= 1 \\ \omega_{y_2}^- &\leq 11 \end{aligned}$$

c) For the average tablet thickness, which is of NTB type, the membership function, μ_{y_3} , is described by:

$$\mu_{y_3} = \begin{cases} 0 & y_3 \leq 3.99 \\ 1 - \frac{4.2-y_3}{0.21} & 3.99 \leq y_3 \leq 4.2 \\ 1 - \frac{y_3-4.2}{0.21} & 4.2 \leq y_3 \leq 4.41 \\ 0 & y_3 \geq 4.41 \end{cases}$$

Let $\omega_{y_3}^-$ and $\omega_{y_3}^+$ denote the negative and positive deviation from the thickness target, the y_3 goal constraints are then formulated as:

$$\begin{aligned} y_3 + \omega_{y_3}^- - \omega_{y_3}^+ &= 4.2 \\ \mu_{y_3} + \frac{\omega_{y_3}^-}{0.21} - \frac{\omega_{y_3}^+}{0.21} &= 1 \\ \omega_{y_3}^+, \omega_{y_3}^- &\leq 0.21 \end{aligned}$$

Step 3: Typically, the DM has no information about the exact values of x_1 , x_2 and x_3 . Let $\partial_{x_j}^-$ and $\partial_{x_j}^+$ denote the negative and positive deviations. Therefore, the trapezoidal membership function, μ_{x_j} ; $j=1, \dots, 3$, is utilized to describe the three process variables as follows:

$$\mu_{x_1} = \begin{cases} 0 & x_1 \leq 21 \\ 1 - \frac{22-x_1}{1} & 21 \leq x_1 \leq 22 \\ 1 & 22 \leq x_1 \leq 24 \\ 1 - \frac{x_1-24}{1} & 24 \leq x_1 \leq 25 \\ 0 & x_1 \geq 25 \end{cases}$$

$$\mu_{x_2} = \begin{cases} 0 & x_2 \leq 13 \\ 1 - \frac{14-x_2}{1} & 13 \leq x_2 \leq 14 \\ 1 & 14 \leq x_2 \leq 16 \\ 1 - \frac{x_2-16}{1} & 16 \leq x_2 \leq 17 \\ 0 & x_2 \geq 17 \end{cases}$$

$$\mu_{x_3} = \begin{cases} 0 & x_3 \leq 11 \\ 1 - \frac{12-x_3}{1} & 11 \leq x_3 \leq 12 \\ 1 & 12 \leq x_3 \leq 14 \\ 1 - \frac{x_3-14}{1} & 14 \leq x_3 \leq 15 \\ 0 & x_3 \geq 15 \end{cases}$$

Step 4: Assign weights to the deviations according to their relative significance to the DM. Then write the complete model as follows:

$$\begin{aligned} \text{Minimize } Z &= 0.35(\omega_{y_1}^- - \omega_{y_1}^+) + 0.25\omega_{y_2}^- + 0.15(\omega_{y_3}^- + \omega_{y_3}^+) \\ &+ 0.1(\partial_{x_1}^+ + \partial_{x_1}^- + \partial_{x_2}^+ + \partial_{x_2}^- + \partial_{x_3}^+ + \partial_{x_3}^-) \end{aligned}$$

Subject to:

$$\begin{aligned} x_1 + \partial_{x_1}^- &\geq 22, & x_1 - \partial_{x_1}^+ &\leq 24, \\ \mu_{x_1} + \partial_{x_1}^+ + \partial_{x_1}^- &= 1, & 0 &\leq \partial_{x_1}^+, \partial_{x_1}^- \leq 1, \\ x_2 + \partial_{x_2}^- &\geq 14, & x_2 - \partial_{x_2}^+ &\leq 16, \\ \mu_{x_2} + \partial_{x_2}^+ + \partial_{x_2}^- &= 1, & 0 &\leq \partial_{x_2}^+, \partial_{x_2}^- \leq 1, \\ x_3 + \partial_{x_3}^- &\geq 12, & x_3 - \partial_{x_3}^+ &\leq 14, \\ \mu_{x_3} + \partial_{x_3}^+ + \partial_{x_3}^- &= 1, & 0 &\leq \partial_{x_3}^+, \partial_{x_3}^- \leq 1, \end{aligned}$$

The obtained optimal process conditions were found to be: Feed Speed of 24.28 (rpm), Pressure of 15.169 (KN), and a Turret Speed of 14.42 (rpm). The expected values for the weight, hardness, and thickness are calculated 630 mg, 17 Kp and 4.2 mm, respectively.

IV. RESULTS

Validation experiments are conducted at the combination of optimal factor settings. Then, the $\bar{x}-s$ charts are established for the three quality responses as shown in Fig. 2. These charts are found to be in-control. Table II also displays the estimated *UCL*, *LCL*, and process capability values at the combination of optimal factor settings.

Utilizing the optimal factor settings; Feed speed = 24.28 RPM, Pressure = 15.16 KN, and Turret speed= 14.42 RPM, the \hat{C}_{pk} values for the averages of tablet's of weight, hardness, and thickness are 1.03, 1.42, and 4.45, respectively. The calculated \hat{MC}_{pk} is increased to 1.86. The corresponding improvement ratios were found to be 77.5%, 31.5%, and 61.3%, respectively. Such results will result in significant improvement in quality by reducing the percentage of nonconforming and thereby enhancing productivity.

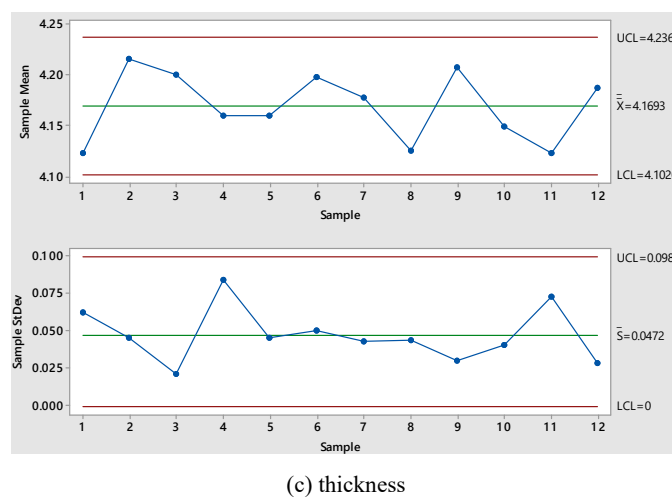
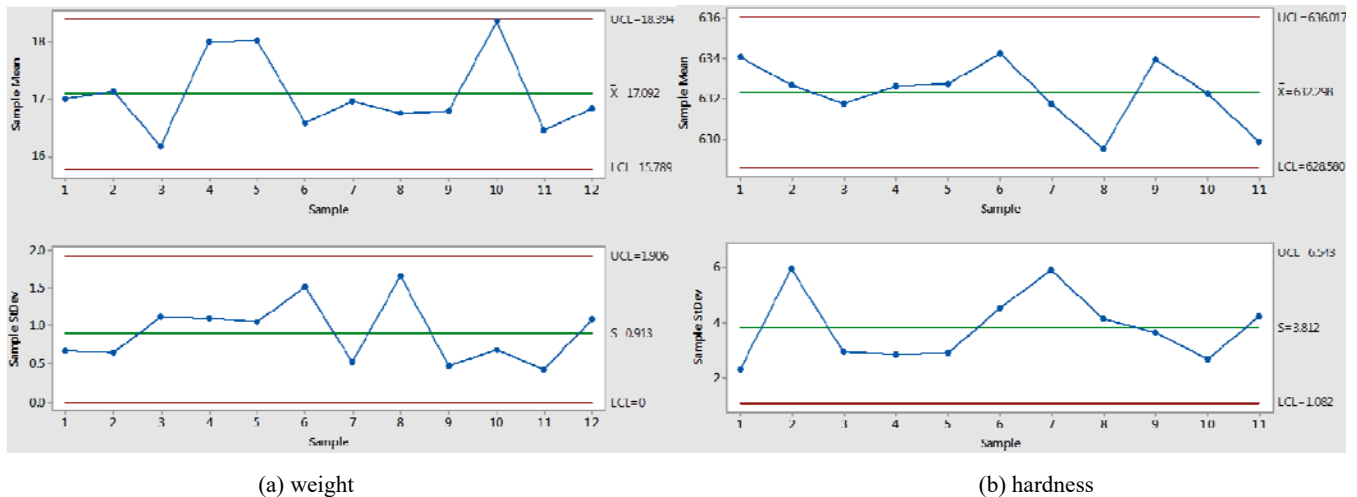


Fig. 2 The \bar{x} -s charts for average tablet at optimal factor settings

REFERENCES

- [1] Al-Refaie A., "FGP model to optimize performance of tableting process with three quality responses," *Transactions of the Institute of Measurement and Control*, Vol. 36(3), 2014b, pp. 336–346.
- [2] Taguchi, G. "Taguchi Methods. Research and Development," Vol. 1, 1991, (American Suppliers Institute Press, Dearborn, Michigan).
- [3] Pignatello, J. J. "Strategies for robust multiresponse quality engineering". *IIE Transactions*, Vol. 25, 1993, pp. 5–15.
- [4] Jean, M. D. and Wang, J. T. "Using a principal component analysis for developing a robust design of electron beam welding". *International Journal of Advanced Manufacturing Technology*, 28, 2006, pp. 882–889.
- [5] Gupta A. Singh H. and Aggarwal A., "Taguchi-fuzzy multi output optimization (MOO) in high speed CNC turning of AISI P-20 tool steel," *Expert Systems with Applications*, Vol. (38), 2011, pp. 6822–6828.
- [6] Candan G. and Yazgan H. "Genetic algorithm parameter optimization using Taguchi method for a flexible manufacturing system scheduling problem," *International Journal of Production Research*, Vol. 53 (3), 2015, pp. 897-915.
- [7] Lin H-C. Su C-T. Wang C-C. Chang B-H. and Juang R-C. "Parameter optimization of continuous sputtering process based on Taguchi methods, neural networks, desirability function, and genetic algorithms," *Expert Systems with Applications*, Vol. 39(17): 2012, pp. 12918–12925.
- [8] Al-Refaie A., M-H Li and K-C. Tai, "Optimizing SUS 304 wire drawing process by grey analysis utilizing Taguchi method," *Journal of University of Science and Technology Beijing, Mineral, Metallurgy, Material*, Vol. 15(6), 2009, pp. 714–722.
- [9] Al-Refaie A., "Optimizing SMT performance using comparisons of efficiency between different systems technique in DEA," *IEEE Transactions on Electronics Packaging Manufacturing*, Vol. 32(4), 2009, pp. 256–264.
- [10] Al-Refaie A., "Super-efficiency DEA approach for optimizing multiple quality characteristics in parameter design. *International Journal of Artificial Life Research*, Vol. 1(2), 2010a, pp. 58–71.
- [11] Al-Refaie A., "A Grey-DEA approach for solving the multiresponse problem in Taguchi Method. *Journal of Engineering Manufacture*," Vol. 224(1), 2010b, pp. 147–158.
- [12] Al-Refaie A., "Optimizing correlated QCHs using principal components analysis and DEA techniques. *Production Planning & Control*," Vol. 22(07), 2011, pp. 676–689.
- [13] Al-Refaie A. and M. Al-Tahat, "Solving the multi-response problem in Taguchi method by benevolent formulation in DEA. *Journal of Intelligent Manufacturing*, Vol. 22(4), 2011, pp. 505–521.
- [14] AL-Refaie A., T. Chen, R. Al-Athamneh, H.C. Wu , " Fuzzy neural network approach to optimizing process performance by using multiple responses," *Journal of Ambient Intelligence and Humanized Computing*, Vol. 7 (6), 2016, pp. 801-816.
- [15] Al-Refaie A. and A. Diabat, "Optimizing convexity defect in a tile industry using fuzzy goal programming," *Measurement, Journal of the International Measurement Confederation*, Vol. 46 (8), 2013, pp. 2807-2815.
- [16] Al-Refaie A., "A proposed satisfaction function model to optimize process performance with multiple quality responses in the Taguchi method. *Journal of Engineering Manufacture*, 2013. doi: 10.1177/0954405413498583.
- [17] Al-Refaie A., "A proposed weighted additive model to optimize multiple quality responses in the Taguchi method with applications,"

- Journal of Process Mechanical Engineering*, Vol. 228(2), 2014a, pp. 291–301.
- [18] Al-Refaie, A., Li, M. H., Jarbo, M., Yeh, C. H., & Bata, N., "Imprecise data envelopment analysis model for robust design with multiple fuzzy quality responses," *Advances in Production Engineering & Management*, Vol. 9(2), 2014a, pp. 83–94.
- [19] Al-Refaie A., W. Al-Alaween, A. Diabat, M.H. Li , "Solving dynamic systems with multi-responses by integrating desirability function and data envelopment analysis," *Journal of Intelligent Manufacturing*, 2014b. doi:10.1007/s10845-014-0986-4.
- [20] Al-Refaie A., "Optimizing multiple quality responses in the Taguchi method using fuzzy goal programming: modeling and applications," *International Journal of Intelligent Systems*, Vol. 30(6), 2015a, pp. 651–675.
- [21] Al-Refaie A., "Optimal performance of plastic pipes' extrusion process using Min-Max model in fuzzy goal programming," *Journal of Process Mechanical Engineering*, 2015b. doi: 10.1177/0954408915620988.