International Journal of Industrial Engineering & Production Research March 2022 Vol. 33, No. 1: 1-18
DOI: 10.22068/ijiepr.33.1.7

RESEARCH PAPER

# Phase I Monitoring of Multivariate Ordinal Based Processes: The MR and LRT Approaches (A Real Case Study in Drug Dissolution Process)

**Ahmad Hakimi[1], Hiwa Farughi[*2], Amirhossein Amiri[3] & Jamal Arkat[4]**

Received 18 April 2021; Revised 25 December 2021; Accepted 10 January 2022;


**ABSTRACT**
*In some statistical processes monitoring (SPM) applications, relationship between two or more ordinal factors is shown by an ordinal contingency table (OCT) and it is described by the ordinal Log-linear model (OLLM). Newton-Raphson algorithm methods have also been used to estimate the parameters of the log-linear model. In this paper, the OLLM based processes is monitored using multivariate ordinal categorical, which is name MR, and likelihood ratio test (LRT) approaches in Phase I. Some simulation studies are applied to performance evaluation of the proposed approaches in terms of probability of signal under step shifts, drifts and the presence of outliers. Results show that, by imposing the small and moderate shifts in the ordinal log-linear model parameters, the MR statistic has better performance than LRT. In addition, a real case study in dissolution testing in pharmaceutical industry is employed to show the application of the proposed control charts in Phase I.*

**KEYWORDS:** *Ordinal log-linear model; Likelihood ratio test; Statistical process monitoring; Drug dissolution; Phase I.*

## 1. Introduction

SPM has many applications that are not limited to process monitoring and can be used in many cases, including monitoring reliability and availability [1]. One of the most important and widely used parts of SPM is multivariate process monitoring that has been used in various fields [2]. For instance, Noorossana and Khalili [3] proposed two control charts and a combined method to monitor auto-correlated linear profiles by using multivariate linear mixed model in Phase II. Multivariate ordinal process monitoring is a completely new area of research in SPM, articles [4] and [5] presented in the Phase II for the first time. In this procedure, two or more correlated ordinal factors are related and proven by a contingency table called OCT this is modeled with the aid of OLLM. In this section, some applicable researches in the literature are discussed to screen the contingency table primarily based techniques. Many researches have been presented about the applications of contingency tables in real words. In this paper, we divide these applications and literature in to two categories as non-SPC and SPC area. At the following, related researches are stated.

### 1.1. Literature of contingency tables in non-SPC area

Subramanyam and Rao [6] tested the hypothesis of independency for 2×n ordinal contingency tables and computed the odds ratio for special conditions. Beh and Davy [7] proposed new Pearson chi-rectangular statistic for contingency tables with three express factors. Yamamoto and Morakami [8] proposed a version for square OCT. In these studies, the belief of unbalanced everyday distribution became additionally taken into consideration that turned into implemented for caries of the tooth. Observe that, there is no research in OLLM/OCT based strategies monitoring in statistical system monitoring and just, a few researchers offered the nominal

* Corresponding author: *Hiwa Farughi*
*h.farughi@uok.ac.ir*

1. *Department of Industrial Engineering, Faculty of Engineering, University of Kurdistan, Sanandaj, Iran.*
2. *Department of Industrial Engineering, Faculty of Engineering, University of Kurdistan, Sanandaj, Iran.*
3. *Department of Industrial Engineering, Faculty of Engineering, Shahed University, Tehran, Iran.*
4. *Department of Industrial Engineering, Faculty of Engineering, University of Kurdistan, Sanandaj, Iran.*

contingency table primarily based methods tracking. On this region, Zhen and Basawa [9] offered a time-dependent contingency table known as the specific time collection table. Ghoreishi and Alijani [10] proposed a technique to forecast the changing patterns of communique variables the use of dynamic contingency table. Kieffer et al. [11] used a contingency table offered through Kijima and Matsui [12] to assess the results of genetic characteristic of 10,000 sufferers on the cancer incidence.

## 1.2. Literature of contingency tables in SPC area

A Multivariate specific method become proposed by means of Yashchin [13] to display the MNP with unexpected parameters the usage of the generalized probability ratio check statistic in phase II. The overall performance of the proposed method become evaluated by the use of a real case observe in semiconductor production device. Li et al. [14] proposed a EWMA-GLRT to monitor the log-linear model based processes in Phase II. Li et al. [15] proposed an incorporated multivariate spatial-signal take a look at and EWMA scheme to screen the shape parameters of the multivariate nonparametric techniques in Phase II. Li et al. [16] proposed a sturdy scheme for tracking the multivariate multinomial strategies by thinking about correlation between specific elements in Phase II. A GLT statistic to reveal the MNP methods turned into presented by means of in Phase II [17]. Then, they blended GLT with an EWMA statistic to improve the overall performance of GLT in detecting small and slight shifts in multinomial multivariate primarily based tactics. In addition, they recognized the parameter(s) accountable for out-of-control (OC) conditions using GLT statistic in Phase II. Kamranrad et al. [18] proposed Wald and Stuart rating check (SST) methods to monitor the nominal contingency tables based totally methods in Phase II. They supplied EWMA-Wald and EWMA-SST information to higher the performance of them proposed manipulate schemes in small and moderate shifts inside the contingency table cells parameter. Further, a diagnostic scheme to diagnose the mobile(s) accountable for OC situation changed into presented in this studies. Effects confirmed that, EWMA-Wald manipulate chart had higher performance than the EWMA-SST and EWMA-GLT in all shifts in nominal log-linear version parameters. Kamranrad et al. [19] proposed Phase I manage scheme to screen the nominal log-linear strategies based totally on SLRT and F manipulate charts and evaluated the noted strategies beneath unique steps, drifts and outlier in nominal log-linear model parameters. Similarly, they advanced SLRT scheme to alternate point estimation in NLLM parameters. Moreover, to reveal the strength of proposed manipulate chart in real area, they applied an information set in health-take care of Urology patients and appropriate outcomes are observed.

A simple ordinal categorical statistic to screen the univariate ordinal procedures to locate the modifications of region first proposed through in Phase II [20]. Wang et al [4] proposed OLLM based methods monitoring statistics including MOC and LMBM in Phase II. They showed that MOC control chart outperforms the LMBM manage charts below one of a kind shifts in the parameters of OLLM. Except, new multivariate ordinal based method known as multivariate ordinal-normal statistic (MONS) became brought by [5]. Additionally, the performance of the MONS approach became in comparison with the MG-p technique and outcomes showed the superiority of the MONS method under the small and slight shifts in OLLM parameters.

Based totally on research in related literature, there may be no take a look at on phase I tracking of OLLM-based totally techniques, while, in maximum instances, the parameters are unknown and we do not have any statistics about the steadiness of the technique. Subsequently, the goal of this paper is proposing a few methods to display the ordinal log-linear tactics in Phase I. The primary problem in Phase I tracking of the OLLM is estimating of the corresponding parameters. As a result, in this paper, a parameter estimation algorithm for OLLM, which is developed of the Newton-Raphson (see [21]). Similarly, MR and LRT statistics are evolved to reveal the OLLM- based processes in phrases of power criterion.

A new EWMA control scheme to monitor the social network with multinomial categorical data has been developed by Perry [22]. This scheme could useful to organization's stakeholders when interest lies in monitoring for shifts in the general health of the organization. Li et al. [23] presented nonparametric KNN-ECUSUM control chart to monitor the multivariate processes by using mixed IC and OC data. Note that, this scheme is the machine leaning based black-box control chart and it is utilized for dimension reduction to transform multivariate data into univariate data. Xiang et al. [24] proposed new control scheme to monitor the multivariate categorical process with

a sparse contingency table. To this aim, they combined the LASSO and Ridge methods to estimate the contingency table distribution and propose the useful EWMA chart.

As stated in above sections, there is no theoretical and applicable research for ordinal contingency table based processes monitoring in Phase I. Hence, in this paper, two new categorical multivariate statistics including MR and LRT have been developed to monitor the OLLM based processes in Phase I. In addition, to show the applications of presented methods, a real case study in pharmaceutical industry based on dissolution process is used which are stated as the novelty of this paper.

The rest sections of this paper is as follows: within the next segment, we assessment the OLLM method tracking records. The Newton-Raphson set of rules to estimate the parameters of the OLLM is discussed in section 3. Phase I monitoring schemes for OLLM approaches are offered in phase 4. Simulation experiment consequences of the proposed records are presented in segment 5. Further, overall, performance of the proposed records is evaluated primarily based on facts set in drug dissolution process and the associated effects are suggested in segment 6. Eventually, the conclusion and future research are stated in section 7.

## 2. Multivariate Ordinal Processes

The OCT is applied to display the multivariate ordinal processes with two or more ordinal variables. This table is used to show the relation between ordinal variables and characterizes the association patterns between the ordinal factors and modeled by the OLLM [5].

### 2.1. The ordinal log-linear model

As stated, the OCT is used to represent the simultaneous relationship between two or more ordinal variables. Consider $p$ variables such as $y_1, y_2, ..., y_p$ each with $h_i$, $i = 1, 2, ..., p$ possible levels. Then, $h_1 \times h_2 \times ... \times h_p$ possible counts of the OCT cells are assumed. The OLLM has been developed to model the relationship between the levels of ordinal factors and the associated frequencies in each cell. The general OLLM form for contingency table with two ordinal factors is defined as follows:

$$\log \mu_{ij} = \mu + \alpha_i + \beta_j + \varphi(u_i - \bar{u})(v_j - \bar{v}), \quad (1)$$

where, $\mu_{ij} = N\pi_{ij}$ is the expected frequency of the cell $(i,j)$ and $u_i = i$ and $v_j = j$ are the row and column scores, respectively. Furthermore, $\mu$ is the overall effect, $\alpha_i$ and $\beta_j$ are the $i$th row and $j$th column effects, respectively. Note that, $\varphi$ is a linear by linear interaction parameter in OLLM which can be estimated by Equation (2):

$$\log\left(\frac{\mu_{ij}\,\mu_{i+1.j+1}}{\mu_{i.j+1}\,\mu_{i+1.j}}\right) = \varphi(u_i - u_{i+1})(v_j - v_{j+1}), \quad (2)$$

where, $(u_i - u_{i+1}) = 1$ and $(v_j - v_{j+1}) = 1$. Note that, according to unknown parameters for monitoring of Phase I, we estimate the parameters of the OLLM by iterative Newton's single-dimensional algorithm presented by [21]. Also, the OLLM for two factors is defined as:

$$\log \boldsymbol{\mu} = \beta_0 + \beta_1 y_1 + \beta_2 y_2 + \varphi(y_1 - \bar{y}_1)(y_2 - \bar{y}_2). \quad (3)$$

where, $\boldsymbol{\mu}$ is the vector of expected frequencies for OCT and $\bar{y}_i$ $(i = 1, 2)$ is the mean of the $i$th ordered variable.

### 2.2. The generalized ordinal log-linear model

The generalized log-linear model for $p$ ordinal variables can be stated by the following equation:

$$\begin{aligned}\log \boldsymbol{\mu} = {} & \beta_0 + \beta_1 y_1 + \beta_2 y_2 + ... + \beta_p y_p + \varphi_{12}(y_1 - \bar{y}_1)(y_2 - \bar{y}_2) + ... + \varphi_{1p}(y_1 - \bar{y}_1)(y_p - \bar{y}_p) + ... \\ & + \varphi_{2p}(y_2 - \bar{y}_2)(y_p - \bar{y}_p) + ... + \varphi_{p-1,p}(y_{p-1} - \bar{y}_{p-1})(y_p - \bar{y}_p) + \varphi_{123}(y_1 - \bar{y}_1)(y_2 - \bar{y}_2)(y_3 - \bar{y}_3) + ... \\ & + \varphi_{p-2,p-1,p}(y_{p-2} - \bar{y}_{p-2})(y_{p-1} - \bar{y}_{p-1})(y_p - \bar{y}_p) + ... + \varphi_{1,...,p-1,p}(y_1 - \bar{y}_1)...(y_{p-1} - \bar{y}_{p-1})(y_p - \bar{y}_p)\end{aligned} \quad (4)$$

where, $\bar{y}_i$ $(i = 1, 2, ..., p)$ is the mean of the $i$th ordinal factor.

As stated before, in Phase I monitoring, the parameters of the OLLM are unknown and ought to be anticipated. As a result, on this paper, we use a parameter-estimating algorithm for OLLM based on aggregate of the Newton-Raphson methods [21, 26]. Be aware that, Newton-Raphson technique is used to estimate the intercept and slope parameters for person results and estimate the interplay coefficients in OLLM,

which might be supplied at the subsequent section.

## 3. The OLLM Parameters Estimation

As mentioned before, the OLLM based process parameters are unknown in Phase I monitoring and should be estimated. In this section, Newton-Raphson algorithm [21] methods are applied to estimate the log-linear model parameters. First the Newton-Raphson algorithm is used to estimate the intercept and the slope parameters of individual effects. This algorithm is as the following equation:

$$\hat{\boldsymbol{\beta}}^{(t+1)} = \hat{\boldsymbol{\beta}}^{(t)} + \left[\mathbf{X}^T \, diag\left(\hat{\boldsymbol{\mu}}^{(t)}\right)\mathbf{X}\right]^{-1} \mathbf{X}^T \left(\mathbf{n} - \hat{\boldsymbol{\mu}}^{(t)}\right), \qquad (5)$$

where $\hat{\boldsymbol{\beta}}^{(t+1)}$ is the ($t$+1)th vector of the OLLM estimated parameters and $\hat{\boldsymbol{\beta}}^{(0)}$ is the primal estimation of $\boldsymbol{\beta}$ which can be estimated through ordinary least squares method or accord values [26]. Furthermore, $\mathbf{X}$ is defined as design matrix (without interaction values of the ordinal factors) and $\mathbf{n}$ is the observation vector of the OCT such that $\mathbf{n}^{\mathbf{T}}\mathbf{1} = N$. Besides, $\hat{\boldsymbol{\mu}}^{(t)} = \exp(\mathbf{X}\hat{\boldsymbol{\beta}}^{(t)})$, where, $\hat{\boldsymbol{\mu}}^{(t)}$ is the estimated vector of expected frequencies in OCT. If $\left\|\hat{\boldsymbol{\beta}}^{(t)} - \hat{\boldsymbol{\beta}}^{(t-1)}\right\| / \left\|\hat{\boldsymbol{\beta}}^{(t-1)}\right\| \le \varepsilon$, where $\left\|\hat{\boldsymbol{\beta}}^{(t)}\right\|$ is the Euclidean norm of the $t$th iteration of estimated parameter and $\varepsilon$ is defined as the small value (in this paper, $\varepsilon = 10^{-5}$), then $\hat{\boldsymbol{\beta}} = \hat{\boldsymbol{\beta}}^{(t)}$ is the desired parameter estimate. In addition, method [21] is used to estimate the interaction coefficients based on equation (6). Note that, two separate methods including Newton-Raphson and one-dimensional Newton-Raphson algorithms should be applied to estimate all parameters of OLLM based parameters in Phase I.

Suppose that, $n_{ij}$ is the cell frequencies of the OCT (with sample size $N$) and the correspondeing expected value is $f_{ij}$. Then, $\hat{\varphi}_N$ is estimated recursively based on Equation (6) through the Newton's method.

$$\hat{\varphi}_N^{(t+1)} = \hat{\varphi}_N^{(t)} + \frac{\sum_{i=1}^{I}\sum_{j=1}^{J}(u_i - \bar{u})(v_i - \bar{v})(n_{ij} - f_{ij}^{(t)})}{\sum_{i=1}^{I}\sum_{j=1}^{J}(u_i - \bar{u})^2 (v_i - \bar{v})^2 f_{ij}^{(t)}}, \qquad (6)$$

where, $f_{ij} = \alpha_i . \beta_j \exp\left[\varphi(u_i - \bar{u})(v_i - \bar{v})\right]$. When $\left|\hat{\varphi}_N^{(t+1)} - \hat{\varphi}_N^{(t)}\right| < \varepsilon$, the algorithm is stopped and desirable $\hat{\varphi}_N$ is obtained. For more information see [25]. Note that, parameters vector of the OLLM is defined as $[\hat{\boldsymbol{\beta}}, \hat{\varphi}_N]$.

## 4. The OLLM Based Processes Monitoring In Phase I

In this section, the LRT and MR statistics are developed for Phase I monitoring of the OLLM based processes. The necessity of this research is to develop the OLLM based processes monitoring which is not presented with any researchers in the literature. The main questions in this paper is, which control charts are suitable for monitoring the OLLM based processes in Phase I and how can the situation of the process be monitored with these control charts with regards to in-control or out-of-control conditions. To answer this question, we first use mentioned parameter estimation to model the OCT based data (called as OLLM) in Phase I. Then, two new statistics including LRT and MR are developed to monitor the mentioned process and performance of these methods are evaluated through Type I error criterion.

### 4.1. The likelihood ratio test based method

Kamranrad et al. [19] used this method for Phase I in nominal variables. In this subsection, the LRT scheme is evolved to screen the OLLM in Phase I. $m$ OCTs with total size equal to $N$ are considered. The LRT procedure is that, at first, all of $m$ OCTs with the same dimension are merged and a unique OCT with the sample size $mN$ is generated. In the second step, OCT $m_1$ is considered as in-control sample and other $m_2$ to $m$ OCTs should be considered as the out-of-control samples to obtain the maximum Likelihood estimators (MLE) of the parameters of the OLLM. This process continues until the $m_1$ to $m_{th\text{-}1}$ OCTs became a single merged sample to obtain the MLE of the OLLM parameters. The LRT statistic to test the $H_0 : \boldsymbol{\beta}_1 = \boldsymbol{\beta}_2 = \ldots = \boldsymbol{\beta}_m$ hypothesis, versus $H_1 : otherwise$, is as follows:

$$LRT_{m_1} = -2(l_0 - l_a), \qquad (7)$$

$$l_a = (l_1 + l_2), \qquad (8)$$

where $l_0$, $l_1$ and $l_2$ are the log-likelihood functions for all OCTs, before and after the change point, respectively. It is noted that OLLM

follows the multinomial distribution with parameters $(N, \pi_{ij})$ presented in Equation 9.

$$p(n_{ku}, k=1,...,m, u=1,...,(k_1 \times ... \times k_p)) = \frac{(N!)^m}{\prod_{k=1}^{m}\prod_{u=1}^{k_1 \times ... \times k_p} n_{ku}!} \prod_{k=1}^{m}\prod_{u=1}^{k_1 ... k_p} \tilde{\pi}_{ku}^{n_{ku}}, \quad (9)$$

Therefore, the log-likelihood function for two categorical variables with *I* and *J* levels and the *m* samples is as follows:

$$l_0 = m\log(N!) - \sum_{k=1}^{m}\sum_{u=1}^{k_1 ... k_p} \log(n_{ku}!) + \sum_{k=1}^{m}\sum_{u=1}^{k_1 ... k_p} \left(n_{ku} \log(\tilde{\pi}_{ku}^{n_{ku}})\right), \quad (10)$$

where,

$$\tilde{\pi}_{ku} = \frac{\exp(\mathbf{x}_u \tilde{\boldsymbol{\beta}})}{\sum_{u=1}^{k_1 ... k_p} \exp(\mathbf{x}_u \tilde{\boldsymbol{\beta}})}, \; for\, k = 1,2,...,m \; and \; u = 1,2,...,(k_1 \times ... \times k_p).$$

$\mathbf{x}_u$ is a vector including *u*th cell of the *x* values and $\tilde{\boldsymbol{\beta}}$ is the parameter estimated vector of the OLLM with *m* contingency tables. In addition, $l_0$ is computed by using Equation (10). Hence, $l_1$ and $l_2$ can also be calculated by Equation (11):

$$\begin{aligned} l_1 &= m_1 \log(N!) - \sum_{k=1}^{m_1}\sum_{u=1}^{k_1 ... k_p} \log(n_{ku}!) + \sum_{k=1}^{m_1}\sum_{u=1}^{k_1 ... k_p} \left(n_{ku} \log(\tilde{\pi}_{ku}^{(1)})\right), \\ l_2 &= (m - m_1)\log(N!) - \sum_{k=m_1+1}^{m}\sum_{u=1}^{k_1 ... k_p} \log(n_{ku}!) + \sum_{k=m_1+1}^{m}\sum_{u=1}^{k_1 ... k_p} \left(n_{ku} \log(\tilde{\pi}_{ku}^{(2)})\right), \end{aligned} \quad (11)$$

where, $\tilde{\pi}_{ku}^{(1)}$ and $\tilde{\pi}_{ku}^{(2)}$ are the *u*th (*u*=1,2, …,( $k_1 \times ... \times k_p$ )) cell probabilities in the *k*th (*k*=1,2,…,*m*) OCT based on the $m_1$ and $m$-$m_1$ OCT, respectively. For more information can see [19]. The standardized $LRT_{m_1}$ statistic using Equation (10) is following equation:

$$SLRT_{m_1} = \frac{LRT_{m_1} - E\left(LRT_{m_1}\right)}{std\left(LRT_{m_1}\right)} \quad (12)$$

where $E\left(LRT_{m_1}\right)$ and $std\left(LRT_{m_1}\right)$ are the mean and the standard deviation values of the $LRT_{m_1}$ for the in-control process and are obtained using simulation. Hence, we should calculate $SLRT_{m_1}$ for all $m_1$ ( $m_1 = 1,...,m-1$ ). The *SLRT* control chart signals when $Max(SLRT_{m_1}) > UCL$ . The UCL is also computed to acquire a certain Type-I error through 10,000 simulation runs.

### 4.2. The *MR*-statistic

Hakimi et al. [25] proposed this method for monitoring OLLM in Phase II. Consider *m* OCTs with *p* ordinal variables (*p*-way OCT) each with $h_1$, $h_2$,…, $h_p$ categories. Hence, the known in-control probabilities for the ordinal cell count is

$$\hat{\pi}_{ij...p,\vartheta}^{(0)} = \frac{f(i,j,k,...,p,\vartheta)}{\sum_{i=1}^{h_1}\sum_{j=1}^{h_2}\sum_{k=1}^{h_3}...\sum_{p=1}^{h_p} f(i,j,k,...,p,\vartheta)}, \forall \vartheta = 1,2,...,m \; ,$$

where, $f(i,j,k,...,p,\vartheta)$ is the corresponding value for cell (*i*,*j*,*k*,…,*p*) for the $\vartheta$ th contingency table. Now, the modified $R_i$ charting statistic for MOC ( $MR_{t,\vartheta}$ ) is defined as:

$$MR_{t,\vartheta} = \left| \sum_{i=1}^{h_1}\sum_{j=1}^{h_2}\sum_{k=1}^{h_3}...\sum_{p=1}^{h_p} (F_{ijk...p-1,\vartheta}^{(0)} + F_{ijk...p,\vartheta}^{(0)} - 1) z_{ijk...p,\vartheta} \right|, \quad (13)$$

where, $F_{ijk...p,\vartheta}^{(0)} = \sum_{i=1}^{h_1}\sum_{j=1}^{h_2}\sum_{k=1}^{h_3}...\sum_{p=1}^{h_p} \pi_{ijk...p,\vartheta}^{(0)}$ . In addition, $\mathbf{z}_{t,\vartheta}$ is:

$$\mathbf{z}_{t,\vartheta} = a_{0,t,\lambda}^{-1} \sum_{s=1}^{t} (1-\lambda)^{t-s} \mathbf{n}_{t,\vartheta}, \tag{14}$$

where, $a_{t_1,t_2,\lambda}^{-1} = \sum_{t=t_1+1}^{t_2} (1-\lambda)^{t_2-t_1}$ and

$$\mathbf{n}_{t\vartheta} = [n_{111\ldots1t,\vartheta}\ n_{112\ldots1t,\vartheta} \ldots n_{11h_3\ldots h_pt,\vartheta}\ n_{121\ldots1t,\vartheta} \ldots n_{12h_3\ldots h_pt,\vartheta} \ldots n_{h_1h_21\ldots1t,\vartheta} \ldots n_{h_1h_2h_3\ldots h_pt,\vartheta}]$$

For more information can see [25]. At any time, if $MR_{t,\vartheta} > L$ the process is out-of-control. Note that, $L$ is the upper control limit of $MR$ control chart and it is calculated to gain a certain Type-I error probability through 10,000 simulation studies.

## 5. The Computational Studies

In this section some simulation experiments are performed to evaluate and compare the performances of the two proposed control charts in terms of signal probabilities under step shifts, drift and outliers. Results are calculated by using 10,000 runs of simulation studies by the MATLAB software. The historical in-control OCT is reported in Table 1.

**Tab. 1. The Phase I in-control OCT**

| $x_1$ | $x_2$ | | | | $n_{i+}$ |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | |
| 1 | 2 | 5 | 1 | 8 | 16 |
| 2 | 5 | 3 | 0 | 7 | 15 |
| 3 | 1 | 3 | 9 | 6 | 19 |
| $n_{+j}$ | 8 | 11 | 10 | 21 | 50 |

The IC parameters of the OLLM based on the above table are estimated as $\hat{\beta}_0 = -0.3767$, $\hat{\beta}_1 = -0.0582$, $\hat{\beta}_2 = -0.1535$ and $\hat{\beta}_{12} = 0.5884$. Hence, the IC ordinal log-linear model in Phase-I monitoring is as follows: $Log\,\mu_{ijk} = -0.3767 - 0.0582 y_i - 0.1535 y_j + 0.5884 y_i y_j;\ i = 1,2,3,\ j = 1,\ldots,4$. Furthermore, the covariance matrix of the OLLM parameters could be estimated by $\mathrm{cov}(\hat{\boldsymbol{\beta}}) = \{\mathbf{X}^T\ [\mathbf{diag}(\hat{\boldsymbol{\mu}}) - \hat{\boldsymbol{\mu}}\,\hat{\boldsymbol{\mu}}^T / N\ ]\mathbf{X}\}^{-1}$, Hence, the standard deviation of the OLLM parameters is as the following vector: $\hat{\boldsymbol{\sigma}}_{0\hat{\beta}} = [1.58, 0.97, 0.89, 0.69]$, where, 1.58, 0.97 and 0.89 are the standard deviation of the intercept parameter, the first and the second slope parameters of the OLLM, respectively. In addition, 0.69 is the parameter $\varphi$ for the interaction of both ordinal factors in the OLLM.

### 5.1. The LRT and *MR* control charts performance evaluation

As mentioned, in this paper, *SLRT* method is used to monitor the OLLM in Phase I. Hence, the mean and the standard deviation values of $LRT_{m_1}$ are computed through 10,000 runs and simulation results are presented in Table 2.

**Tab. 2. The in-control $E\left(LRT_{m_1}\right)$ and $std\left(LRT_{m_1}\right)$ for *I*=3, *J*=4 and *k*=20**

| $m_1$ | $E\left(LRT_{m_1}\right)$ | $std\left(LRT_{m_1}\right)$ | $m_1$ | $E\left(LRT_{m_1}\right)$ | $std\left(LRT_{m_1}\right)$ |
|---|---|---|---|---|---|
| 1 | 2536.34 | 21.85 | 11 | 2537.97 | 22.20 |
| 2 | 2537.85 | 22.03 | 12 | 2637.56 | 22.41 |
| 3 | 2537.01 | 21.72 | 13 | 2536.72 | 21.84 |
| 4 | 2536.23 | 21.24 | 14 | 2536.69 | 21.61 |
| 5 | 2536.34 | 20.28 | 15 | 2537.62 | 21.17 |
| 6 | 2536.69 | 21.52 | 16 | 2537.82 | 21.96 |
| 7 | 2536.19 | 21.47 | 17 | 2536.45 | 22.05 |
| 8 | 2535.76 | 21.25 | 18 | 2536.48 | 21.86 |
| 9 | 2537.51 | 22.09 | 19 | 2536.99 | 21.62 |
| 10 | 2538.07 | 22.58 | 20 | - | - |

The *UCL*s of the SLRT and *MR* charts are calculated equal to 10.90 and 12.57 to obtain Type-I error of 0.05. Then, control charts performance is evaluated under different step shifts, drift and in the presence of outliers in the OLLM parameters. To impose shift, the IC parameter vector, $\boldsymbol{\beta}^{(0)}$ changes to $\boldsymbol{\beta}^{(1)} = \boldsymbol{\beta}^{(0)} + \mathbf{d}$ where $\mathbf{d} = (\delta_1 \sigma_{\beta_0}, \delta_2 \sigma_{\beta_1}, \delta_3 \sigma_{\beta_2}, \delta_4 \varphi)$ and $\delta_j$, $j = 1,2,3,4$, is the shift values in the OLLM parameters corresponding to their standard deviations. For the step shift, a shift is imposed in the parameter vector $\boldsymbol{\beta}$, from $(\tau+1)\,th$ sample up to the end. For the drift shift, the first $r-1$ samples are assumed in-control and are generated using the log-linear parameter vector of $\boldsymbol{\beta}^{(0)}$. The change in the parameter vector starts from $r$th sample, where the imposed shift in the $r$th sample after change point is obtained by $\boldsymbol{\beta}_r^{(1)} = \boldsymbol{\beta}^{(0)} + \frac{r-1}{m-1}\mathbf{d}$, $r = \tau+1, \ldots, m$. In the case of shift with outliers, we select random different percent of OLLM (5%, 10% and 25%) and then generate with OC parameters vector $\boldsymbol{\beta}^{(1)}$ ( $\boldsymbol{\beta}^{(1)} = \boldsymbol{\beta}^{(0)} + \mathbf{d}$ ). The SLRT and the *MR* control charts performance under different step shifts at $\tau = 2, 5$ and 10 are evaluated and shown in Tables 3-5, respectively.

**Tab. 3. The SLRT and the *MR* control charts performance under different step shifts at $\tau = 2$**

| | d | 0.05 | 0.1 | 0.2 | 0.3 | 0.5 | 0.8 | 1 | 1.5 | 2 |
|---|---|---|---|---|---|---|---|---|---|---|
| Intercept | LRT | 0.0758 | 0.0918 | 0.2105 | 0.4551 | 0.6546 | 0.8125 | 0.9508 | 1.000 | 1.000 |
| | MR | 0.0899 | 0.1059 | 0.2985 | 0.5087 | 0.7091 | 0.8315 | 0.9512 | 1.000 | 1.000 |
| First slope | LRT | 0.0801 | 0.0987 | 0.2051 | 0.3992 | 0.6023 | 0.7995 | 0.9355 | 1.000 | 1.000 |
| | MR | 0.0858 | 0.1009 | 0.2274 | 0.4891 | 0.6251 | 0.8025 | 0.9241 | 1.000 | 1.000 |
| Second slope | LRT | 0.0769 | 0.0951 | 0.2008 | 0.4878 | 0.6218 | 0.8415 | 0.9451 | 1.000 | 1.000 |
| | MR | 0.0805 | 0.1124 | 0.2150 | 0.5011 | 0.6981 | 0.8507 | 0.9502 | 1.000 | 1.000 |
| $\varphi$ | LRT | 0.0689 | 0.0902 | 0.2225 | 0.4015 | 0.6098 | 0.9005 | 1.000 | 1.000 | 1.000 |
| | MR | 0.0804 | 0.1012 | 0.2895 | 0.4981 | 0.6271 | 0.8975 | 0.9981 | 1.000 | 1.000 |

**Tab. 4. The SLRT and the *MR* control charts performance under different step shifts at $\tau = 5$**

| | d | 0.05 | 0.1 | 0.2 | 0.3 | 0.5 | 0.8 | 1 | 1.5 | 2 |
|---|---|---|---|---|---|---|---|---|---|---|
| Intercept | LRT | 0.0662 | 0.0811 | 0.1152 | 0.2975 | 0.4876 | 0.7514 | 0.8802 | 0.9982 | 1.000 |
| | MR | 0.0715 | 0.0887 | 0.1565 | 0.3024 | 0.4990 | 0.7721 | 0.8911 | 0.9993 | 1.000 |
| First slope | LRT | 0.0624 | 0.0809 | 0.1089 | 0.2879 | 0.4784 | 0.7589 | 0.8271 | 0.9514 | 1.000 |
| | MR | 0.0704 | 0.0875 | 0.1337 | 0.2997 | 0.4960 | 0.7975 | 0.8567 | 0.9582 | 1.000 |
| Second slope | LRT | 0.0635 | 0.0821 | 0.1102 | 0.2899 | 0.4796 | 0.7868 | 0.8504 | 0.9528 | 1.000 |
| | MR | 0.0710 | 0.0878 | 0.1398 | 0.3017 | 0.5007 | 0.7924 | 0.8489 | 0.9511 | 1.000 |
| $\varphi$ | LRT | 0.0650 | 0.0812 | 0.1945 | 0.2901 | 0.4927 | 0.7917 | 0.8667 | 0.9815 | 1.000 |
| | MR | 0.0722 | 0.0833 | 0.1992 | 0.3014 | 0.4993 | 0.7867 | 0.8540 | 0.9702 | 1.000 |

**Tab. 5. The SLRT and the *MR* control charts performance under different step shifts at $\tau = 10$**

| | d | 0.05 | 0.1 | 0.2 | 0.3 | 0.5 | 0.8 | 1 | 1.5 | 2 |
|---|---|---|---|---|---|---|---|---|---|---|
| Intercept | LRT | 0.0653 | 0.0795 | 0.1019 | 0.2667 | 0.4772 | 0.7334 | 0.8662 | 0.9526 | 1.000 |
| | MR | 0.0702 | 0.0829 | 0.1318 | 0.2973 | 0.4952 | 0.7509 | 0.8597 | 0.9410 | 1.000 |
| First slope | LRT | 0.0600 | 0.0801 | 0.1012 | 0.2521 | 0.4691 | 0.7215 | 0.8316 | 0.9417 | 1.000 |
| | MR | 0.0693 | 0.0866 | 0.1296 | 0.2764 | 0.4782 | 0.7339 | 0.8320 | 0.9102 | 0.9991 |
| Second slope | LRT | 0.0603 | 0.0814 | 0.1023 | 0.2569 | 0.4759 | 0.7511 | 0.8445 | 0.9501 | 1.000 |
| | MR | 0.0688 | 0.0854 | 0.1308 | 0.2782 | 0.4822 | 0.7439 | 0.8381 | 0.9237 | 1.000 |
| $\varphi$ | LRT | 0.0633 | 0.0825 | 0.1893 | 0.2769 | 0.4836 | 0.7805 | 0.8616 | 0.9637 | 1.000 |
| | MR | 0.0697 | 0.0830 | 0.1916 | 0.3002 | 0.4912 | 0.7838 | 0.8329 | 0.9267 | 0.9995 |

As shown in Tables 3-5, as the grandeur of the step shifts in OLLM parameters increases, the power of LRT and *MR* charts is improved. In addition, results show that under the *MR* chart has better performance than the SLRT control

charts under small and moderate step shifts in all OLLM parameters.

Moreover, the proposed control charts performances under drifts based on the $\boldsymbol{\beta}_r^{(1)} = \boldsymbol{\beta}^{(0)} + \frac{r-1}{m-1}\mathbf{d}$, $r=\tau+1,\ldots, m$ are evaluated and presented in Tables 6 to 8. Note that, the change points are considered as $\tau = 2,5 \text{and } 10$.

**Tab. 6. The SLRT and the *MR* control charts performance under drifts at $\tau = 2$**

| | d | 0.05 | 0.1 | 0.2 | 0.3 | 0.5 | 0.8 | 1 | 1.5 | 2 |
|---|---|---|---|---|---|---|---|---|---|---|
| Intercept | LRT | 0.0744 | 0.0892 | 0.1979 | 0.3011 | 0.5207 | 0.7825 | 0.8960 | 0.9431 | 1.000 |
| | MR | 0.0818 | 0.0956 | 0.2028 | 0.3159 | 0.5993 | 0.7963 | 0.8821 | 0.9267 | 1.000 |
| First slope | LRT | 0.0751 | 0.0933 | 0.1567 | 0.2670 | 0.4963 | 0.7613 | 0.8823 | 0.9397 | 1.000 |
| | MR | 0.0796 | 0.0969 | 0.1639 | 0.2935 | 0.5037 | 0.7584 | 0.8631 | 0.9159 | 0.9968 |
| Second slope | LRT | 0.0755 | 0.0958 | 0.1631 | 0.2776 | 0.4990 | 0.7692 | 0.8909 | 0.9439 | 1.000 |
| | MR | 0.0797 | 0.1003 | 0.1792 | 0.2863 | 0.5167 | 0.7731 | 0.8810 | 0.9381 | 0.9990 |
| $\varphi$ | LRT | 0.0769 | 0.0991 | 0.1834 | 0.2867 | 0.5100 | 0.7932 | 0.9002 | 1.000 | 1.000 |
| | MR | 0.0834 | 0.1008 | 0.1992 | 0.2993 | 0.5297 | 0.7809 | 0.8893 | 0.9826 | 1.000 |

**Tab. 7. The SLRT and *MR* control charts performance under drifts at $\tau = 5$**

| | d | 0.05 | 0.1 | 0.2 | 0.3 | 0.5 | 0.8 | 1 | 1.5 | 2 |
|---|---|---|---|---|---|---|---|---|---|---|
| Intercept | LRT | 0.0615 | 0.0802 | 0.0994 | 0.1347 | 0.3348 | 0.6649 | 0.7991 | 0.9942 | 1.000 |
| | MR | 0.0691 | 0.0862 | 0.1035 | 0.1489 | 0.3507 | 0.6642 | 0.7895 | 0.8966 | 0.9931 |
| First slope | LRT | 0.0611 | 0.0796 | 0.0952 | 0.1296 | 0.3289 | 0.6517 | 0.7829 | 0.9939 | 1.000 |
| | MR | 0.0701 | 0.0823 | 0.1008 | 0.1367 | 0.3418 | 0.6605 | 0.7803 | 0.9015 | 0.9983 |
| Second slope | LRT | 0.0616 | 0.0799 | 0.0991 | 0.1303 | 0.3302 | 0.6909 | 0.7901 | 0.9925 | 1.000 |
| | MR | 0.0700 | 0.0820 | 0.1012 | 0.1411 | 0.3469 | 0.6885 | 0.7886 | 0.9124 | 0.9990 |
| $\varphi$ | LRT | 0.0621 | 0.0784 | 0.1399 | 0.1967 | 0.3455 | 0.6881 | 0.8021 | 0.9993 | 1.000 |
| | MR | 0.0687 | 0.0799 | 0.1468 | 0.2004 | 0.3509 | 0.6924 | 0.7993 | 0.9438 | 1.000 |

**Tab. 8. The SLRT and *MR* control charts performance under drifts at $\tau = 10$**

| | d | 0.05 | 0.1 | 0.2 | 0.3 | 0.5 | 0.8 | 1 | 1.5 | 2 |
|---|---|---|---|---|---|---|---|---|---|---|
| Intercept | LRT | 0.0653 | 0.0795 | 0.1019 | 0.2667 | 0.4772 | 0.7334 | 0.8662 | 0.9526 | 1.000 |
| | MR | 0.0702 | 0.0829 | 0.1318 | 0.2973 | 0.4952 | 0.7509 | 0.8597 | 0.9410 | 1.000 |
| First slope | LRT | 0.0602 | 0.0736 | 0.0993 | 0.1220 | 0.3682 | 0.7158 | 0.8269 | 0.9338 | 0.9997 |
| | MR | 0.0637 | 0.0822 | 0.1010 | 0.1295 | 0.3798 | 0.7208 | 0.8230 | 0.9104 | 0.9980 |
| Second slope | LRT | 0.0606 | 0.0766 | 0.0921 | 0.1307 | 0.3798 | 0.7232 | 0.8375 | 0.9394 | 1.000 |
| | MR | 0.0642 | 0.0824 | 0.1018 | 0.1310 | 0.4002 | 0.7089 | 0.8261 | 0.9111 | 0.9958 |
| $\varphi$ | LRT | 0.0612 | 0.0778 | 0.1002 | 0.1386 | 0.3896 | 0.7505 | 0.8413 | 0.9408 | 1.000 |
| | MR | 0.0645 | 0.0799 | 0.1098 | 0.1402 | 0.4011 | 0.7483 | 0.8038 | 0.9196 | 0.9937 |

The results from Tables 6-8 show that when $\tau = 2,5 \text{and } 10$, the *MR* control chart signals faster than the SLRT chart under small and moderate drifts in the OLLM parameters. In addition, Figures. 1-12, compare the SLRT and *MR* control charts performances under the different presence of outliers in terms of the signal probability criterion by considering 5%, 15% and 25% outliers in the OCTs. Those analysis have be done for four parameters in OLLM, that means for intercept, first and second slope and $\varphi$.

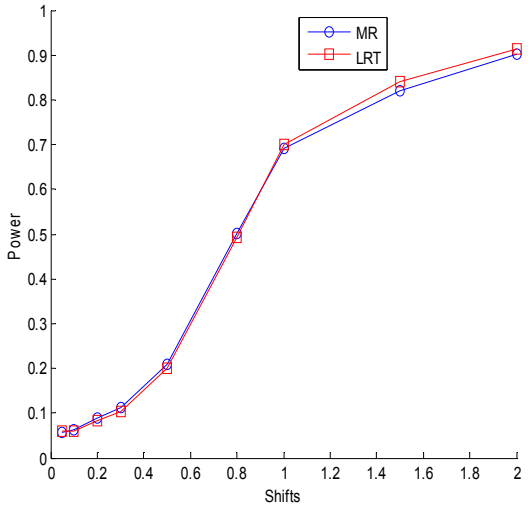


**Fig. 1. Comparing the SLRT and *MR* control charts performance under 5% outliers in the intercept**

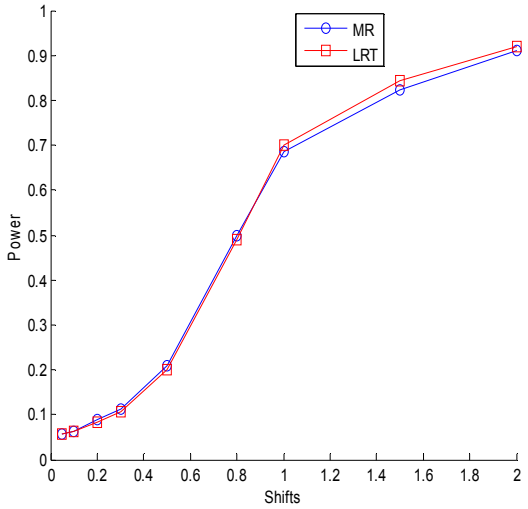


**Fig. 2. Comparing the SLRT and *MR* control charts performance under 5% outliers in the first slope**

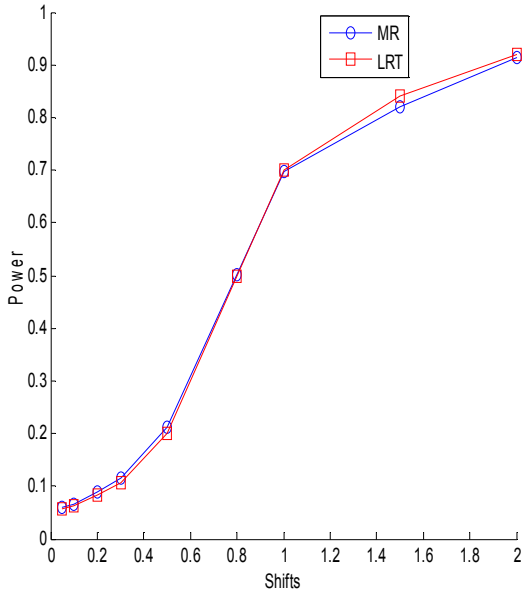


**Fig. 3. Comparing the SLRT and *MR* control charts performance under 5% outliers in the second slope**

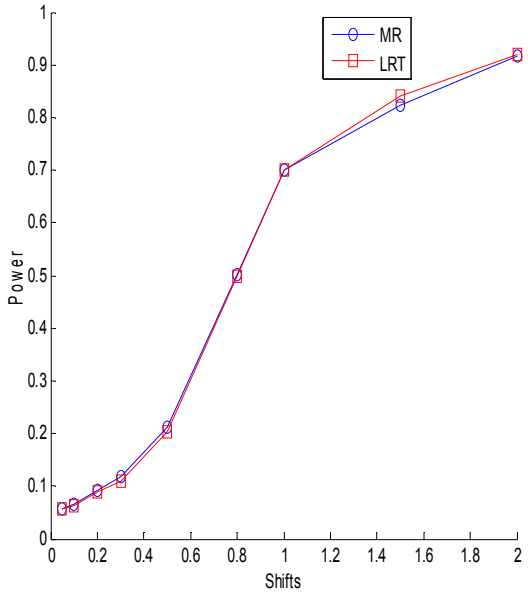


**Fig. 4. Comparing the SLRT and *MR* control charts performance under 5% outliers in the $\varphi$**

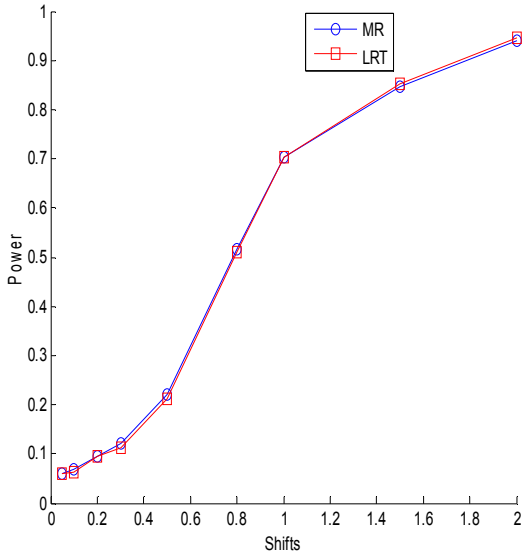


**Fig. 5. Comparing the SLRT and *MR* control charts performance under 15% outliers in the intercept**

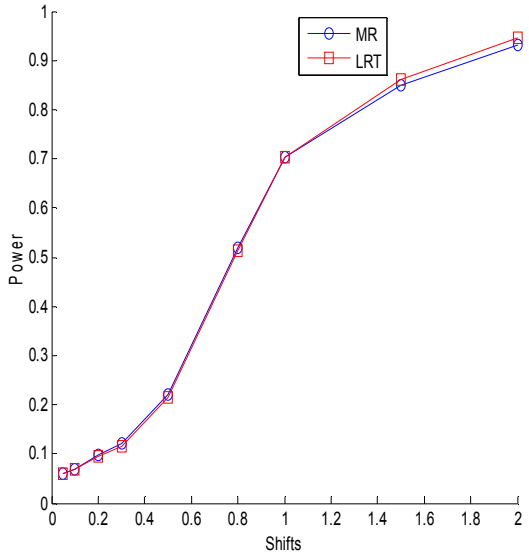


**Fig. 6. Comparing the SLRT and *MR* control charts performance under 15% outliers in the first slope**

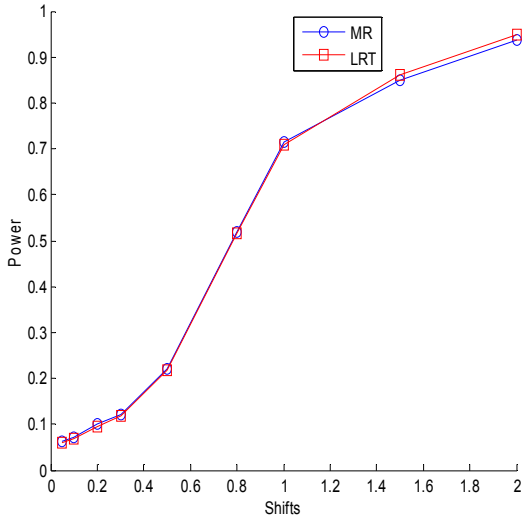


**Fig. 7. Comparing the SLRT and *MR* control charts performance under 15% outliers in the second slope**

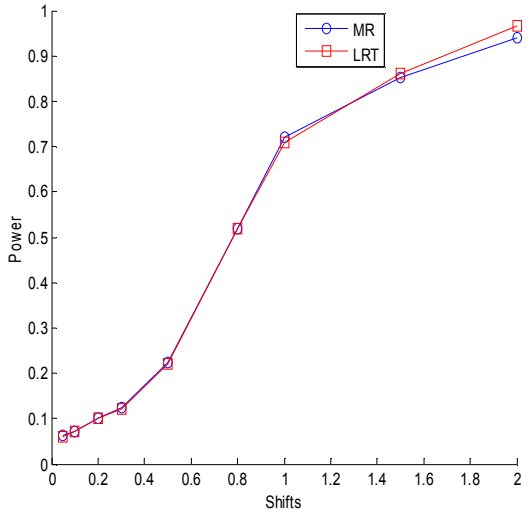


**Fig. 8. Comparing the SLRT and *MR* control charts performance under 15% outliers in the $\varphi$**

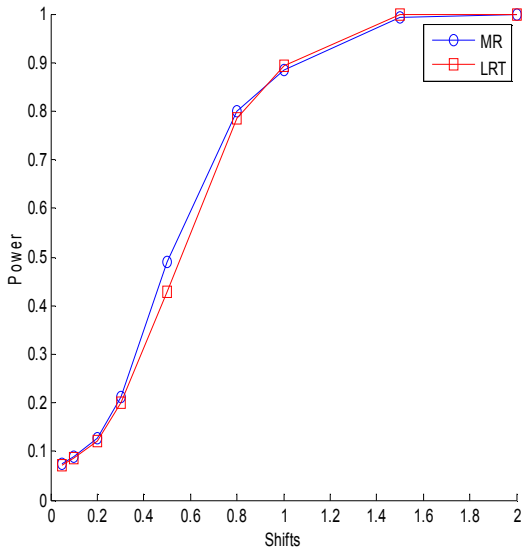


**Fig. 9. Comparing the SLRT and *MR* control charts performance under 25% outliers in the intercept**

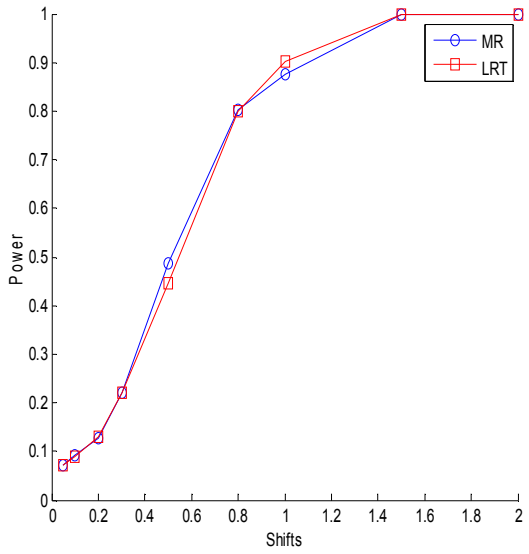


**Fig. 10. Comparing the SLRT and *MR* control charts performance under 25% outliers in the first slope**

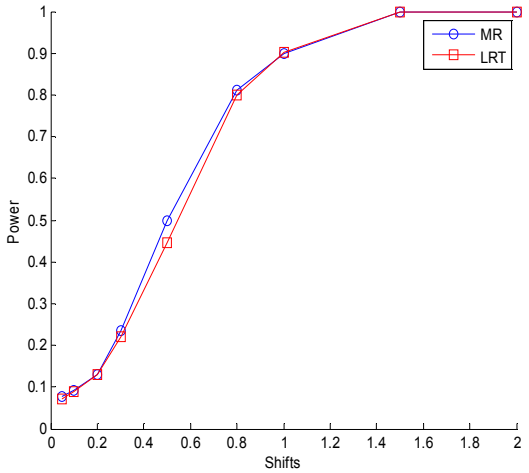


**Fig. 11. Comparing the SLRT and *MR* control charts performance under 25% outliers in the second slope**

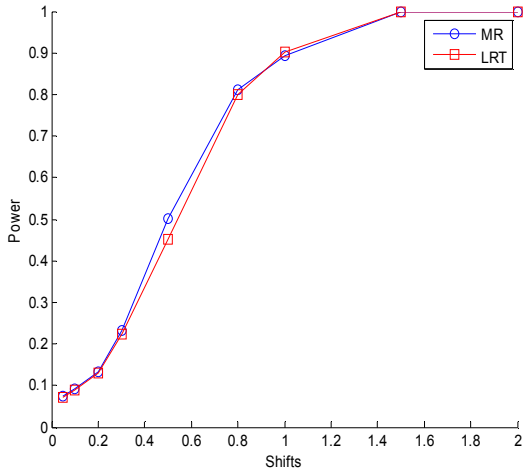


**Fig. 12. Comparing the SLRT and *MR* control charts performance under 25% outliers in the $\varphi$**

As it is clear from Figures. 1-12, the *MR* control chart has better performance than the SLRT method in detecting OC condition under the different presence of outliers based on small and moderate shifts in OLLM parameters.

## 6. A Real Case In Drug Dissolution

The process by which a solid dissolved substance enters into a solution is called dissolution. In the medicinal industry, it can be specified as "the rate of medication substance that penetrates into solution under standardized status of liquid/solid juncture, temperature and solvent compound each unit of time". Dissolution is regarded as one of the most significant tests for controlling quality conducted on prescribed amount as in medicine and is now changing to an instrument for forecasting the extent and rate which a drug becomes available in a physiologically active form, and in some cases, replacing clinical studies to designate bioequivalence. Dissolution conduct of medications affect their pharmacological activity. According to [28] the test for medication dissolution in this industry is

regularly utilized to provide critical in vitro drug release information aimed at controlling the quality, i.e., to estimate batch-to-batch stability of solid oral dose types such as pills, and medication progression, i.e., to foresee in vivo drug release profiles. Three special conditions are available in which dissolution testing functions as a substantial role: (a) decision making based on the preparation and optimization: while developing the products where dissolution efficiency is a substantial feature of the quality; both preparing the product and the procedure for manufacturing are optimized on the bases of arriving at particular dissolution objectives. (b) Equivalence decisions: within the advancement of generic product, as well as the time of conducting the procedure after approval or preparation shifts, resemblance of in vitro dissolution characteristics between the reference product and its generic or changed type are one of the main needs for decisions of regulative approval. (c) Decisions based on the product reception and release: while the process of manufacturing in a usual way, most of the time dissolution results are one of the yardsticks applied to make product release decisions [29,30,31].

As Gray et al. [32] put, four various dissolution apparatus are used in order to promote a suitable dissolution technique for solid-dose compositions dependent upon the properties of medication product. Apparatus 1 and 2 are the most widely used techniques in dissolution testing. Apparatus 1 includes a container composed of glass or any other static, crystalline substance and a cylindrical basket stuck to the bottom of a rotational mixer. The installation for Apparatus 2 is commonly similar to Apparatus 1 except that a paddle with a blade and a shaft is used as the mixing part. For dose types, sinkers can be used that would float under other circumstances.

These apparatuses have characteristics such as simplicity, robustness, being well standardized, and flexibility to permit dissolution testing for different types of solid-dosage forms [33]. The third Apparatus is developed in order to diagnose the requirement for a system that changes the dissolution situations to mimic the gastrointestinal tract in a consecutive manner, so that in vitro-in vivo connection can be created. Apparatus 3 contains a series of cylindrical, crystalline containers with a flat bottom, a series of crystalline reciprocating cylinders with static accessories and screens at the top and bottom of the cylinders, a motor, and a drive assembly to reciprocate the cylinders which are vertically inside the containers; and if desired, the reciprocating cylinders can be moved horizontally to different rows of the vessels. Gray et al [32] pointed out that Apparatus 4 is composed of a repository containing the dissolution instrument, a pump that drives the instrument atop through the flow-cell in a vertical mode, and a water bath to retain the temperature of the dissolution instrument. Apparatus 1 to 4 are shown in the following Figures for dissolution testing to control the quality of processes [34,35,36].

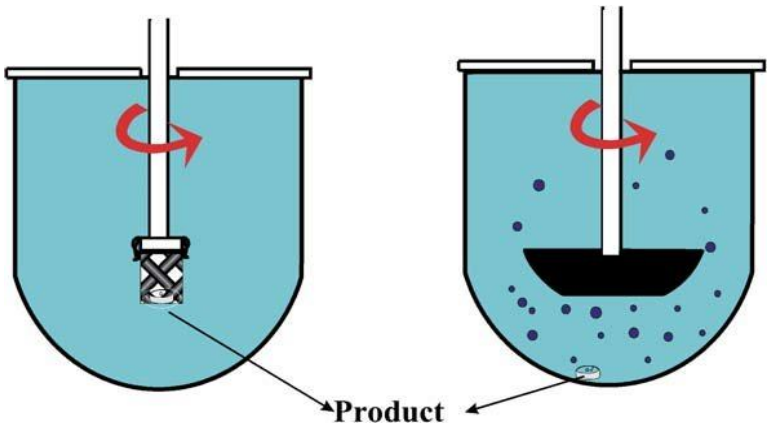


**Fig. 13. Schematic representation for Apparatuses 1 and 2 for drug dissolution testing [34]**

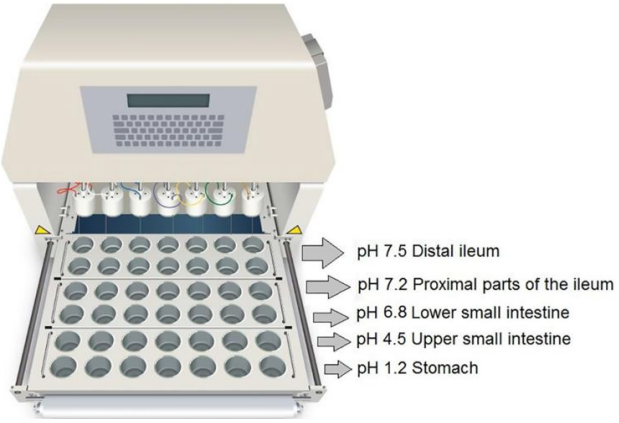


**Fig. 14. Apparatus 3 in drug dissolution testing [35]**

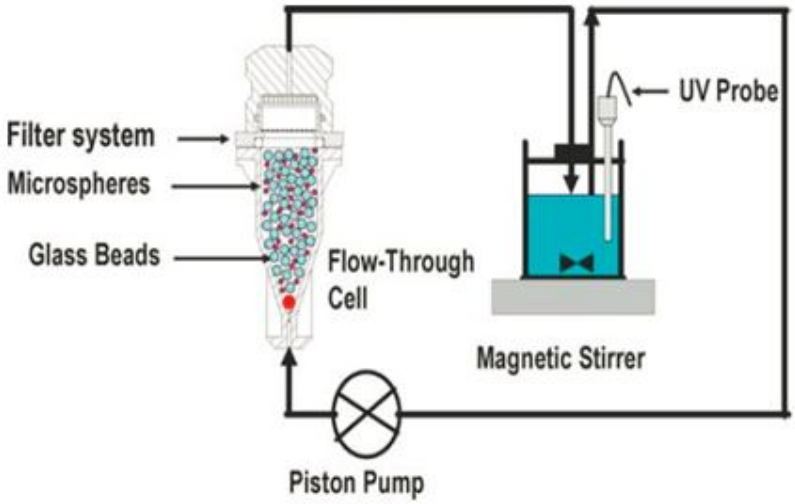


**Fig. 15. Apparatus 4 in drug dissolution testing [36]**

In this paper, drug dissolution process for a pharmaceutical company in Iran is monitored for five periods including initial time, first, second, third and sixth months in Phase I. In this application, a three-way contingency table with three categorical variables including time, release percent and potential of hydrogen (PH) is designed. Note that, time is categorized into four categories as 10, 30, 45 and 60 minutes. Release percent includes two categories as "> 85" and "> 100" and PH is also categorized into four categories as 1.2, 4.5, 6.8 and 7.A real data set is collected based on five contingency tables according to dissolution results from a research and development (R&D) laboratory of mentioned pharmaceutical company. Note that, five real contingency tables are presented in Appendix A.

### 6.1. Performance evaluation

In this subsection, the *MR* and the SLRT control charts are used to obtain whether the OLLM based process is in control or not. The UCLs of the mentioned LRT and MR charts are set equal to 23.11 and 30.76, respectively, to obtain the false alarm probability of $\alpha = 0.05$. Figures 16, shows the SLRT statistics for five real OCTs.

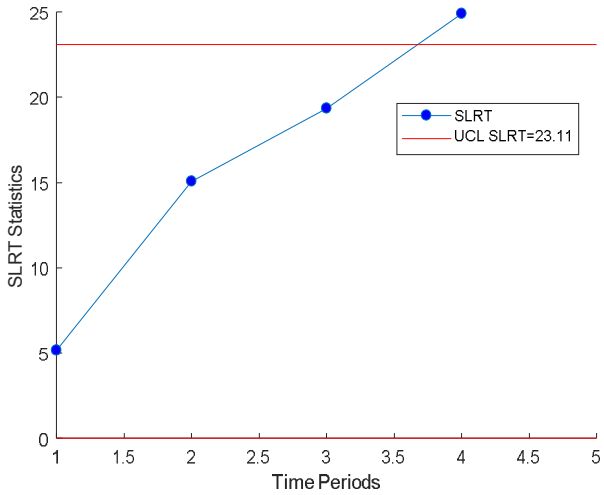


**Fig. 16. The SLRT control chart for drug dissolution**

Above control chart shows the OC condition at sample number 4. Therefore, the corresponding assignable causes for this signal should be recognized and removed. In addition, the *MR* statistic is equal to 36.14. Which is longer than the corresponding UCL and shows that the process is out-of-control.

## 7. Concluding Remarks

In present paper, we developed two OCTs based control charts including SLRT and *MR* for Phase I monitoring the OLLM based processes. Performances of the proposed charts are evaluated through some simulation studies and results were reported in terms of the probability of signal under different step shifts, drift and outliers. Results showed that the *MR* chart outperform the SLRT chart under small and moderate shifts in all parameters of the OLLM (Note that, this sentence is the answer of the main question of this paper). In addition, a real data set in dissolution testing process in pharmaceutical industry was applied to show the utility of the proposed control charts in Phase I. For future research, investigation of the Phase I diagnostic scheme for out-of-control condition can be proposed. In addition, developing change point estimation method to find the real time of the change in OLLM is suitable item for future research.

## Acknowledgment

The authors thank the staff of Pars Darou Company, especially Dr. Hakimi, for their help and cooperation.

## References

[1] Farughi, H., Hakimi, A., Kamranrad, R. *"Availability Prediction of the Repairable Equipment using Artificial Neural Network and Time Series Models"*, International Journal of Industrial Engineering & Production Research, Vol. 29, No. 1, (2018), pp. 79-90.

[2] Noorossana, R., Saghaei, A., Izadbakhsh, H., Aghababaei, O. *"Monitoring Multinomial Logit Profiles via Log-Linear Models"*, International Journal of Industrial Engineering & Production Research, Vol. 24, No. 2, (2013), pp. 137-142.

[3] Noorossana, R., Khalili, S. *"Phase II monitoring of auto-correlated linear profiles using multivariate linear mixed model"*, International Journal of Industrial Engineering & Production Research, Vol. 32, No. 1, (2021), pp.1-11.

[4] Wang, J., Li, J., Su, Q. "*Multivariate ordinal categorical process control based on log-linear modeling*," Journal of Quality Technology, Vol. 49, No. 2, (2017), pp.108-122.

[5] Hakimi, A., Farughi, H., Amiri, A. "*New Phase II Control Chart for Monitoring Ordinal Contingency Table based Processes*," Journal of Industrial and Systems Engineering. Vol. 12, (2019), pp. 15-34.

[6] Subramanyam, K., Rao, M.B. "*Analysis of odds ratios in 2×n ordinal contingency tables,"* Multivariate Statistics and Probability. Vol. 27, No. 1, (1989), pp. 505-520.

[7] Beh, E.J., Davy, P.J. "*Theory & Methods: Partitioning Pearson's Chi-Squared Statistic for a Completely Ordered Three-Way Contingency Table,*" Australian & New Zealand Journal of Statistics. Vol. 40, No. 4, (1998), pp. 465-477.

[8] Yamamoto, K., Murakami, H. *"Model based on skew normal distribution for square contingency tables with ordinal categories,"* Computational Statistics & Data Analysis. Vol. 78, No. 1, (2014), pp. 135-140.

[9] Zhen, X., Basawa, I.V. *"Categorical time series models for contingency tables,"* Statistics & Probability Letters, Vol. 79, No. 10, (2009), pp. 1331-1336.

[10] Ghoreishi, S.K., Alijani, M. *"Dynamic association modeling in 2×2 contingency tables,"* Statistical Methodology, Vol. 8, No. 2, (2011), pp. 242-255.

[11] Kieffer, D., Bianchetti, L., Poch, O. *"Wicker N. Perfect sampling on 2×⋯× 2× K contingency tables with an application to SAGE data,"* Journal of Statistical Planning and Inference, Vol. 142, No. 4, (2012), pp. 896-901.

[12] Kijima, S., Matsui, T. *"Polynomial time perfect sampling algorithm for two-rowed contingency tables,"* Random Structures & Algorithms. Vol. 29, No. 2, (2006), pp. 243-256.

[13] Yashchin, E. *"On detection of changes in categorical data,"* Quality Technology & Quantitative Management. Vol. 9, No. 1, (2012), pp. 79-96.

[14] Li, J., Tsung, F., Zou, C. *"Directional control schemes for multivariate categorical processes,"* Journal of Quality Technology. Vol. 44, No. 2, (2012), pp. 136-154.

[15] Li, Z., Zou, C., Wang, Z., Huwang, L. *"A multivariate sign chart for monitoring process shape parameters,"* Journal of Quality Technology. Vol. 45, No. 2, (2013), pp. 149-165.

[16] Li, J., Tsung, F., Zou, C. *"Directional change-point detection for process control with multivariate categorical data."* Naval Research Logistics (NRL), Vol. 60, No. 2, (2013), pp. 160-173.

[17] Kamranrad, R., Amiri, A., Niaki, S.T.A. *"New Approaches in Monitoring Multivariate Categorical Processes based on Contingency Tables in Phase II,"* Quality and Reliability Engineering International. Vol. 33, No. 5, (2017), pp. 1105-1129.

[18] Kamranrad, R., Amiri, A., Niaki, S.T.A. *"Phase-II monitoring and diagnosing of multivariate categorical processes using generalized linear test-based control charts,"* Communications in Statistics-Simulation and Computation. Vol. 46, No. 8, (2017), pp. 5951-5980.

[19] Kamranrad, R., Amiri, A., Niaki, S.T.A. *"Phase-I monitoring of log-linear model-based processes (a case study in health care: Kidney patients),"* Quality and Reliability Engineering International. Vol. 35, No. 6, (2019), pp. 1766-1788.

[20] Li, J., Tsung, F., Zou, C. *"Multivariate binomial/multinomial control chart."* IIE Transactions. Vol. 46, No. 5, (2014), pp. 526-542.

[21] Agresti, A. Categorical Data Analysis. Department of Statistics University of Florida Gainesville, Florida: John Wiley & Sons, Inc., (2002), Hoboken, New Jersey.

[22] Perry, M. B. *"An EWMA control chart for categorical processes with applications to social network monitoring"*, Journal of Quality Technology, Vol. 52, No. 2, (2020), pp. 182-197.

[23] Li, W., Zhang, C., Tsung, F., Mei, Y. *"Nonparametric monitoring of*

*multivariate data via KNN learning"*, International Journal of Production Research, Vol. 59, No. 20, (2021), pp. 6311-6326.

[24] Xiang, D., Pu, X., Ding, D., Liang, W. *"An efficient charting scheme for multivariate categorical process with a sparse contingency table"*, Journal of Quality Technology, Vol. 53, No. 1, (2021), pp. 88-105.

[25] Hakimi, A., Farughi, H., Amiri, A., Arkat, J. *"Phase II Monitoring of the Ordinal Multivariate Categorical Processes"*, Advances in Industrial Engineering, Vol. 55, No. 3, (2021), pp. 249-267.

[26] Beh, E.J., Farver, T.B. *"An evaluation of non-iterative methods for estimating the linear-by-linear parameters of ordinal log-linear models.*" Australian & New Zealand Journal of Statistics. Vol. 51, No. 3, (2009), pp. 237-249.

[27] Yeh, A.B., Huwang, L., Li, Y.M. *"Profile monitoring for a binary response,"* IIE Transactions, Vol. 41, No. 11, (2009), pp. 931-941.

[28] Bai, G., Wang, Y.P., Armenante, M. *"Velocity profiles and shear strain rate variability in the USP Dissolution Testing Apparatus 2 at Different Impeller Agitation Speeds,"* International Journal of Pharmaceutics. Vol. 403, (2011), pp. 1-14.

[29] Wang, Y., Snee, R.D., Keyvan, G., Muzzio, F.J. "*Statistical comparison of dissolution profiles,"* Drug Development and Industrial Pharmacy. Vol. 42, No. 5, (2016), pp. 796-807.

[30] Anand, O.M., Lawrence, X.Y., Conner, D.P., Davit, B.M. *"Dissolution testing for generic drugs: an FDA perspective."* The AAPS journal. Vol. 13, No. 3, (2011), pp. 328-337.

[31] Zhang, X., Duan, J., Kesisoglou, F., Novakovic, J., Amidon, G.L, Jamei, M., Lionberger, R. *"Mechanistic oral absorption modeling and simulation for formulation development and bioequivalence evaluation: report of an FDA public workshop,"* CPT: pharmacometrics & systems pharmacology. Vol. 6, No. 8, (2017), pp. 492-495.

[32] Gray, V.A., Cole, E., Toma, J.M.R, Ghidorsi, L, Guo, J.H., Han, J.H., Langdon, T. "*Use of enzymes in the dissolution testing of gelatin capsules and gelatin-coated tablets--revisions to Dissolution< 711> and Disintegration and Dissolution of Dietary Supplements< 2040."* Dissolution Technologies. Vol. 21, No. 4, (2014), pp. 6-20.

[33] Martin, G.P., Gray, V.A. *"Overview of Dissolution Instrument Qualification, Including Common Pitfalls,"* Dissolution Technologies. Vol. 18, No. 1, (2011), pp. 6-10.

[34] Qureshi, S.A. *"A new crescent-shaped spindle for drug dissolution testing-but why a new spindle?."* Dissolution Technologies. Vol. 11, No. 1, (2004), pp. 13-21.

[35] Pezzini, B.R., Issa, M.G., Duque, M.D., Ferraz, H.G. *"Applications of USP apparatus 3 in assessing the in vitro release of solid oral dosage forms,"* Brazilian Journal of Pharmaceutical Sciences. Vol. 51, (2015), pp. 265-272.

[36] Zolnik, B.S., Raton, J.L., Burgess, D.J. *"Application of USP apparatus 4 and in situ fiber optic analysis to microsphere release testing,"* Dissolution Technologies. Vol. 12, No. 2, (2005), pp. 11-14.

## Appendix A

## A real case data set (5 periods ordinal contingency table of the drug dissolution)

**Tab. A1. Ordinal contingency table for the initial period**

| | PH | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1.2 | | 4.5 | | 6.8 | | 7 | |
| | Release rate (%) | | | | | | | |
| Time (Min) | >85 | >100 | >85 | >100 | >85 | >100 | >85 | >100 |
| 10 | 199 | 604 | 99 | 450 | 187 | 235 | 96 | 212 |
| 30 | 194 | 305 | 110 | 324 | 87 | 210 | 332 | 567 |
| 45 | 101 | 255 | 205 | 255 | 293 | 202 | 589 | 909 |
| 60 | 589 | 403 | 395 | 310 | 98 | 303 | 295 | 202 |

**Tab. A2. Ordinal contingency table for the first month**

| | PH | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1.2 | | 4.5 | | 6.8 | | 7 | |
| | Release rate (%) | | | | | | | |
| Time (Min) | >85 | >100 | >85 | >100 | >85 | >100 | >85 | >100 |
| 10 | 105 | 582 | 97 | 399 | 199 | 325 | 102 | 155 |
| 30 | 148 | 301 | 302 | 221 | 105 | 215 | 301 | 399 |
| 45 | 98 | 137 | 161 | 304 | 301 | 405 | 601 | 607 |
| 60 | 239 | 401 | 401 | 198 | 101 | 103 | 397 | 208 |

**Tab. A3. Ordinal contingency table for the second month**

| | PH | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1.2 | | 4.5 | | 6.8 | | 7 | |
| | Release rate (%) | | | | | | | |
| Time (Min) | >85 | >100 | >85 | >100 | >85 | >100 | >85 | >100 |
| 10 | 201 | 501 | 159 | 508 | 105 | 301 | 101 | 99 |
| 30 | 122 | 298 | 201 | 301 | 98 | 389 | 301 | 308 |
| 45 | 99 | 304 | 307 | 299 | 268 | 299 | 551 | 700 |
| 60 | 402 | 105 | 402 | 109 | 105 | 302 | 201 | 305 |

**Tab. A4. Ordinal contingency table for the third month**

| | PH | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1.2 | | 4.5 | | 6.8 | | 7 | |
| | Release rate (%) | | | | | | | |
| Time (Min) | >85 | >100 | >85 | >100 | >85 | >100 | >85 | >100 |
| 10 | 101 | 599 | 101 | 503 | 99 | 204 | 102 | 198 |
| 30 | 208 | 94 | 287 | 401 | 121 | 354 | 97 | 608 |
| 45 | 99 | 120 | 301 | 302 | 301 | 298 | 602 | 305 |
| 60 | 217 | 298 | 402 | 209 | 110 | 187 | 301 | 225 |

**Tab. A5. Ordinal contingency table for the sixth month**

| | PH | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1.2 | | 4.5 | | 6.8 | | 7 | |
| | Release rate (%) | | | | | | | |
| Time (Min) | >85 | >100 | >85 | >100 | >85 | >100 | >85 | >100 |
| 10 | 102 | 500 | 100 | 399 | 199 | 196 | 180 | 109 |
| 30 | 121 | 360 | 233 | 405 | 98 | 297 | 302 | 208 |
| 45 | 205 | 231 | 207 | 299 | 302 | 300 | 601 | 699 |
| 60 | 401 | 201 | 406 | 302 | 109 | 301 | 223 | 101 |