Malaya Journal of Matematik, Vol. 9, No. 1, 101-104, 2021
https://doi.org/10.26637/MJM0901/0016

A mathematical model for using fuzzy Weibull distribution for the effect of Cisplatin on lung cancer cell

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Abstract
The reaction of cisplatin on the cell cycle and DNA synthesis of human lung adenocarcinoma cell line PC-9 were analysed by flow cytometry by exposure to cisplatin $(1.0\mu g/ml)$ for 1 and 24 hours revealed a delayed S-phase transit and an gathering of cells in the $G2/M$-Phase.Two type of treatment have been studied with fuzzy failure rate function using fuzzy Weibull distribution.

Keywords
Failure time, fuzzy weibull distribution, PC-9 cell, cell cycle, DNA synthesis rate.

AMS Subject Classification
26A33, 30E25, 34A12, 34A34, 34A37, 37C25, 45J05.

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Article History: Received **12** October **2020**; Accepted **19** December **2020**

Contents

1. Introduction

DNA Replication occurs in multicellular organism during cell division. This occurs during embryogenes is and growth of tissues. In the organism DNA synthesis is a primitive and most important event in animal kingdom. The multiplication of the entire genetic information's in an organism is essential for cell division in living organism. The persistence of DNA over millions of years of animal evolutions and its fundamental role and implies deep protective mechanism to ensure its conservation. Bromodeoxyuridine (Brdurd) is a thymidine chain which is attached into DNA during S-phase of the cell cycle. Gratzner [7] produced a monoclonal antiBrdUrd antibody in 1982 and Dolbeare et. al [4] developed a method for simultaneous flow cytometric measurement of the cellular DNA content and the amount of incorporate Brdurd using an immunofluorescent antibody in 1983. They also showed that Brdurd linked green fluorescence was proportional to the amount of incorporated BrdUrd [4]. Since then, many studies using this antibody have been reported [1, 3, 5, 6, 9, 10, 11]. Dean et. al [3] described that a mean Brdurd linked fluorescence could be taken as an estimate of the mean DNA synthesis rate. Langer et. al [9] reported that the ration of S Phase cells estimated by this method matched well with 3 H-thymidine labelling index. Despite that, there were few studies in which this technique was used to analysis the chemotherapeutic effects on cancer cell Kinetics [6]. In this paper, Fuzzy Failure rate with two parameter weibull distribution for the PC-9 cell growth with different time intervals were discussed. Using two parameter weibull distribution, it is clear that the α-cut for the lower Failure values are increases when t increases. hence the value of α-cut for the upper Failure rate are decreases when t increases.
This shows that if the time increases, the Lower fuzzy weibull distribution for the effect of PC-9 cell growth level increases,

were as the Upper fuzzy weibull distribution for the effect of *PC*-9 cell growth level decreases.

2. Notation

λ - Scale Parameter.

β - Shape Parameter.

$\lambda(\alpha)$ - Alpha cut of Scale Value.

$\beta(\alpha)$ - Alpha cut of Shape Value.

$H(t)$ - Failure rate function.

$\bar{H}(t)$ - Fuzzy Failure rate function.

T - Test termination time.

3. Fuzzy Mathematical Model

The weibull Distribution is widely used in statistical method for life data.

Among all statistical techniques it may be in use for engineering analysis with smaller sample sizes than any other method. A continuous random variable T'' with two parameter weibull distribution $W(\lambda,\beta)$ where $\beta > 0$ is the Shape Parameter, $\lambda > 0$ is the Scale Parameter has the probability distribution,

$$f(t) = \beta\lambda\left(\frac{t}{\lambda}\right)^{\beta-1} e^{\left(\frac{t}{\lambda}\right)^{\beta}},\ t > 0, \lambda \geq 0, \beta \geq 0.$$

The Failure rate function of two parameter weibull distribution,

$$H(t) = \beta\lambda\left(\frac{t}{\lambda}\right)^{\beta-1}.$$

The shape parameter gives the flexibility of weibull distribution by changing the value of shape parameter. It is obvious that $h(t)$ is a decreasing function when $\beta < 1$, constant when $\beta = 1$, and an increasing function when $\beta > 1$. Therefore we consider the Weibull distribution with fuzzy parameter by replacing the scale parameter λ into the fuzzy number $\bar{\lambda}$, shape parameter β into $\bar{\beta}$ for $\alpha \in [0,1]$, the alpha cuts of fuzzy Failure rate function with two parameter weibull distribution is $h(\alpha) = \bar{h}_1(\alpha), \bar{h}_2(\alpha)$, where,

$$\bar{h}_1(t) = \text{Inf}\left\{\beta\lambda\left(\frac{t}{\lambda}\right)^{(\beta-1)},\ t > 0, \bar{\lambda} \in \bar{\lambda}(\alpha), \bar{\beta} \in \bar{\beta}(\alpha)\right\}$$

$$\bar{h}_2(t) = \text{Sup}\left\{\beta\lambda\left(\frac{t}{\lambda}\right)^{(\beta-1)},\ t > 0, \bar{\lambda} \in \bar{\lambda}(\alpha), \bar{\beta} \in \bar{\beta}(\alpha)\right\}$$

4. Application

Let us take an experiment conducted by Toshiaki Fujikane and other (12) on the cell growth curves were shown in fig (1) with treatment for one hour, the cell number increased to 53.9% of the control 72 hour after treatment fig(1a) and the surviving fraction was 0 .61% with treatment for 24 hour, the cell number decreases to 12.3% of the control (1b) and the surviving fraction was zero.

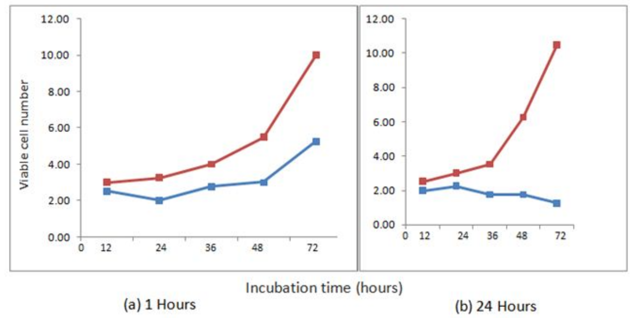

Figure 1

5. Results

Table 1. Fuzzy failure rate function of weibull distribution for the effect of C-DDP on cell survival for 1-hour treatment

α values	HL $(t=1)$	HL $(t=1)$	HU $(t=1)$	HU $(t=1)$
0	0.2217	0.1300	0.0216	0.0163
0.1	0.2045	0.1207	0.0254	0.0186
0.2	0.1880	0.1118	0.0297	0.0212
0.3	0.1724	0.1033	0.0346	0.0242
0.4	0.1575	0.0952	0.0403	0.0274
0.5	0.1436	0.0876	0.0467	0.0311
0.6	0.1305	0.0804	0.0540	0.0352
0.7	0.1183	0.0737	0.0623	0.0397
0.8	0.1069	0.0675	0.0717	0.0447
0.9	0.0965	0.0616	0.0822	0.0502
1	0.0868	0.0562	0.0939	0.0562

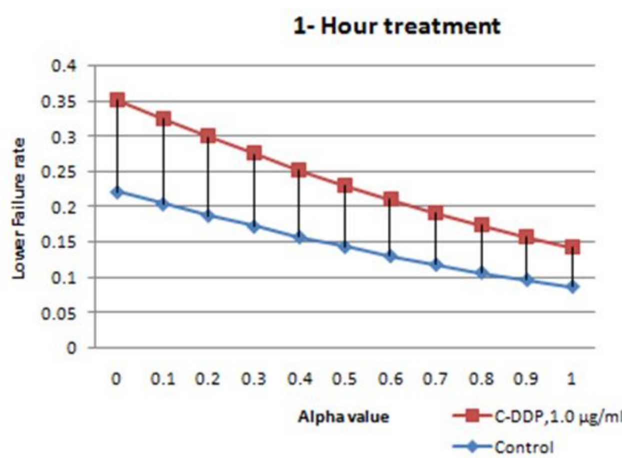

Figure 2. Lower Failure rate of 1-hour C-DDP. $(1.0\mu g/ml)$ treatment

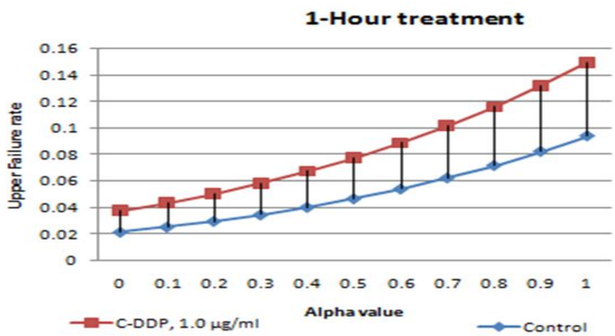

Figure 3. Upper Failure rate of 1-hour C-DDP, $(1.0\mu g/ml)$ treatment.

Table 2. Fuzzy failure rate function of weibull distribution for the effected of $C-DDP$ on cell survival for (2-days) 24-hour treatment:

α values	HL $(t=2)$	HL $(t=2)$	HU $(t=2)$	HU $(t=2)$
0	34.199	0.1853	3.43 E-01	6.14 E-02
0.1	25.989	0.1813	4.17 E-01	6.71 E-02
0.2	18.611	0.1768	5.08 E-01	7.32 E-02
0.3	14.083	0.1719	6.20 E-01	7.97 E-02
0.4	10.8	0.1669	7.57 E-01	8.64 E-02
0.5	8.3649	0.1615	9.27 E-01	9.35 E-02
0.6	6.5609	0.1559	1.14 E+00	1.01 E-01
0.7	5.1818	0.1503	1.40 E+00	1.09 E-01
0.8	4.1252	0.1445	1.73 E+00	1.17 E-01
0.9	3.3016	0.1387	2.14 E+00	1.25 E-01
1	2.6574	0.1328	2.66 E+00	1.33 E-01

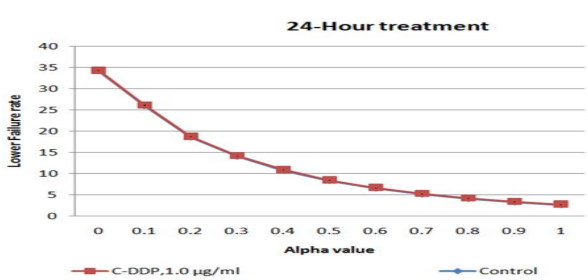

Figure 4. Lower Failure rate of 24-hour C-DDP, $(1.0\mu g/ml)$ treatment.

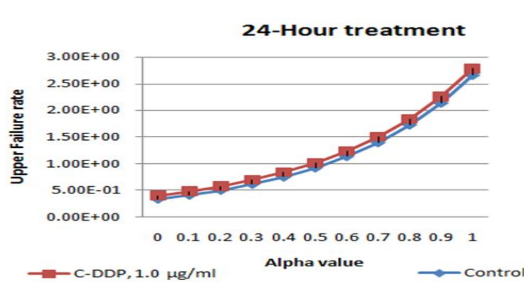

Figure 5. Upper Failure rate of 24-hour C-DDP, $(1.0\mu g/ml)$ treatment

6. Conclusion

In this paper, some results have been discussed. by using two parameter fuzzy weibull distribution of flow cytometric analysis of kinetic reaction of cisplatin on lung cancer cell growth curves shows in table (1) that with treatment for 1-hour, when the alpha-cut increases, the cell number decreases in lower value and increases in upper value. But the percentage of the cell number is 54.6 in the both value, At the same time, the cell growth curves shows in table (2) that with treatment for 24-hour, when the alpha-cut increases, the cell number decreases in lower value and increases in upper value. But the percentage of cell number in both values is 13.28. If the time t is increases then the failure time is also increases.

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ISSN(P):2319 − 3786
Malaya Journal of Matematik
ISSN(O):2321 − 5666
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