## Calotropis gigantea Leaves Extract (CGLE) increases anticancer effect of 5-Fluorouracil and Decreases effect of Doxorubicin on Human Colon Cancer WiDr cell line

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### **Abstract**

- \*Objective: The objective of this study was to examine whether Calotropis gigantea leaf extract (CGLE) synergizes the therapeutic potential of 5-flourouracil and Doxorubicin against colon cancer WiDr cell lines.
- Methods: MTT assay was used to measure the growth inhibitory effect of the combination.

Results: CGLE 3  $\mu$ g/ml which was combined with 5-FU 62.5  $\mu$ g/ml, 125  $\mu$ g/ml, and 250  $\mu$ g/ml, synergistically inhibited the growth of WiDr colon cancer cells line with Combination Index value (CI) ranging from 0.20 to 0.07. In contrast, combination of CGLE with Doxorubicin was given antagonistically inhibited on the growth of colon cancer WiDr cell line, with Combination Index value (CI) ranging from 0,9 to 3,3 (moderate antagonis effect until highly antagonist effect).

- •Conclusion: Combination therapy of CGLE showed strong synergism with 5-FU and strong antagonism with doxorubicin in inhibiting the growth of human colon cancer WiDr cells line,
- \*Keywords: Calotropis gigantea, 5-FU, doxorubicin, colon Cancer Cell Lines, Widr.

### **Background**

In previous study, the ability of Calotropis gigantean leaves extract (CGLE) as an anticancer has been investigated. The result showed that CGLE is cytotoxic to WiDr cell line (IC50:42,2  $\mu$ g/ml) and T47D cell line (IC50:89.75  $\mu$ g/ml). In this study, we investigated the anticancer activity of CGLE in combination with Doxorubicin and 5 Fluorouracil on WiDr cell line.

### **Material and Methods**

MTT assay was used to measure the growth inhibitory effect of the combination. Synergistic efficacy was subjected to median effect analysis with nonexclusive model as previously described by Chou and Talaly

			T		C	GLE : 5-	FU/DOX					
	1	2	3	4	5	6	7	8	9	10	11	12
Α		1/2 IC5	0	½ IC50	CGLE: 10	00 μg/ml	1/2 IC50	CGLE: 50	µg/ml			
В	corr	3/4 BC50 2/4BC50 1/ <sub>8</sub> BC50		<sup>3</sup> / <sub>4</sub> IC50 CGLE : 100 μg/ml <sup>2</sup> / <sub>4</sub> IC50 CGLE : 100 μg/ml <sup>1</sup> / <sub>8</sub> IC50 CGLE : 100 μg/ml			<sup>3</sup> / <sub>4</sub> IC50 CGLE : 50 μg/ml <sup>2</sup> / <sub>4</sub> IC50 CGLE : 50 μg/ml <sup>1</sup> / <sub>8</sub> IC50 CGLE : 50 μg/ml					
C	CGLE									1		
C												
E		100 μg/ml		½ IC50 CGLE : 25 μg/ml ½ IC50 CGLE : 12,5 μg/ml			2,5 µg/ml	CONTROL OF CELL				
F	5-FU/	50 µg/	ml	3/4 IC5	0 CGLE : 2	5 μg/ml	3/4 IC50	CGLE: 1	2,5 µg/ml	CONT	KOL O	CELL
G	DOX	25 µg/	ml	2/ <sub>4</sub> IC5	0 CGLE : 2	5 µg/ml	2/4IC50	CGLE: 1	2,5 µg/ml	CONTROL OF		
н		12.5 mg	/ml	1/, 104	O COLE : 2	Import 2	1/_105	CGLE - I	E: 12,5 μg/ml CON	MEDIA		

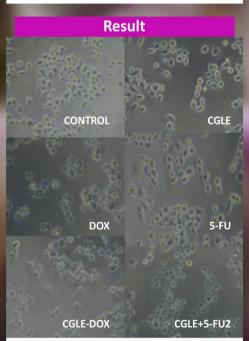
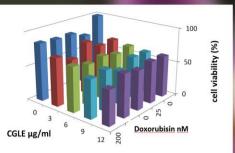


Figure 1.The effect of CGLE, Doxorubicin, 5-FU monotherapy and combination theraphy to morphology of WiDr cell line. Cell morphology was examined by using inverted microcope with magnification 400x

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# Combination Index CGLE with Doxorubisin on WiDr cell line

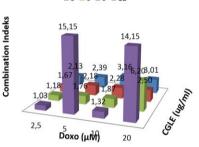
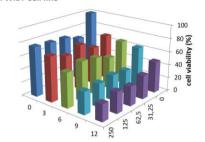


Figure 2. Antagonisme effect of CGLE with Doxorubisin on WiDr Cell line



### Combination Index of CGLE with 5- Fluorouracil on WiDr cell line

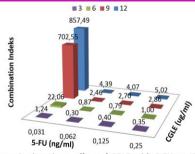
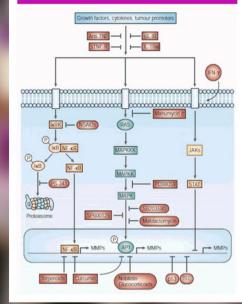


Figure 3. sinergisme effect of CGLE with 5-FU on WiDr Cell line

### Table of cell viability , Combination Index (CI) and effect classification of combination therapy of CGLE extract and 5-Fluorouracil on WiDr cell line

No	Komi	cell	viab	ility	cı	effect		
	CGLE (µg/ml)	5 FU (µg/ml)	rata-rata		± SD			· · ·
1	3	31.25	57.08	±	1.18	1.24	antagonis	
	6	31.25	48.04	±	0.33	22.06	Highly antagonis	
	9	31.25	35.39	±	2.16	702.55	Highly antagonis	
	12	31.25	35.76	±	1.03	857.49	Highly antagonis	
2	3	62.5	68.90	±	0.86	0.3	sinergis	
	6	62.5	56.25	±	2.40	0.87	sinergis ringan	
	9	62.5	37.69	±	5.17	2.46	Highly antagonis	
	12	62.5	29.17	±	4.26	4.39	Extremely antagonis	
3	3	125	60.06	±	3.15	0.4	sinergis	
	6	125	59.59	±	16.99	0.79	Moderate antagonis	
	9	125	34.92	±	2.54	2.7	Highly antagonis	
	12	125	31.42	±	2.09	4.07	Highly antagonis	
4	3	250	68.06	±	3.09	0.35	sinergis	
	6	250	52.43	±	2.79	1	antagonis	
	9	250	33.30	±	2.82	2.86	Highly antagonis	
	12	250	25.30	±	3.64	5.02	Extremely antagonis	

### Discussion



#### Conclusion

Combination therapy of CGLE showed strong synergism with 5-FU and strong antagonism with doxorubicin in inhibiting the growth of human colon cancer WiDr cells line

### **Acknowledgment**

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### Calotropis gigantea (widuri)

