Appendix II In Vivo Combinations.

Example II-A. In Vivo 2-Drug Combinations Against House Flies.

Table for Original Data and Summary of Results.

Lethal Toxicity of rotenone and pyrethrins to houseflies: Constant ratio combination of R:P at 1:5 and 1:15 (**For Details of Analysis see Appendix I Example A. CompuSyn Report**)

(Adopted from Table 19 of Pharmcol Rev. 58: 621-681, 2006)

Original data[a,c]			CompuSyn generated results[b]										
Compound or mixture	Concentration (μg/ml)	% Kill	Dose-effect parameters			Combination index at				Dose-reduction index at			
			m	D_m	r	ED_{50}	ED_{75}	ED_{90}	ED_{95}	ED_{50}	ED_{75}	ED_{90}	ED_{95}
	0.1	26.0											
	0.15	47.5											
Rotenone (R)	0.20	67.5	2.626	0.151	0.907								
	0.25	81.5											
	0.35	89.5											
	0.5	21.5											
	0.75	39.5											
Pyrethrins (P)	1.0	54.0	2.387	0.893	0.995								
	1.5	75.0											
	2.0	89.0											
Rotenone	0.3	27.0								2.01	1.97	1.94	1.92
+	0.45	53.0											
Pyrethrins	0.60	64.0	2.519	0.450	0.994					2.38	2.44	2.50	2.54
	0.875	82.0		(0.075									
(1R:5P)	1.175	93.0		+ 0.375)		0.9176	0.9163	0.9155	0.9152				
Rotenone	0.4	23.0								3.70	3.64	3.59	3.55
+	0.6	48.0											
Pyrethrins	0.8	61.0	2.533	0.652	0.983					1.46	1.50	1.54	1.57
	1.2	76.0		(0.041									

(1R:15P)	1.6	93.0	+ 0.611)	0.9543	0.9465	0.9274	0.9187

[a] Original data from Le Pelley and Sullivan (1936), retrieved and analyzed by Finney (1952), analyzed by Chou and Talalaly (1987).
[b] Further analyzed by CompuSyn (Chou and Martin, 2005).
[c] Data for rotenone or pyrethrins alone were the average of two series of experiments. F_a (fractional kill) = % kill/100

Conclusions/Comments by T.C. Chou for example II-A:

1. **The r values showed excellent experimental data, especially for the *in vivo* experiments.**
2. **The D_m (LD_{50} in ug/ml) values showed that Rotenone is 5.9-fold more potent than Pyrethrins. It is remarkable that the choice of R:P of 1:5 and 1:15 experiments were conducted in animals three quarter of a century ago in 1936. These are the brilliant choices.**
3. **Both R:P at 1:5 and 1:15 combinations showed slight synergism (at nearly additive effect). The quantitative CI values showed 1:15 has slightly more synergy than the 1:5 ratio combination. The early speculative debate on whether synergism by Finney half a century ago in 1952, turned out to be quite valid and now confirmed by the quantitative CI method with computerized simulation.**
4. **The DRI values show all combination data above showed favorable dose-reductions with DRI > 1.**