



# A non-fatal self-poisoning attempt with sildenafil

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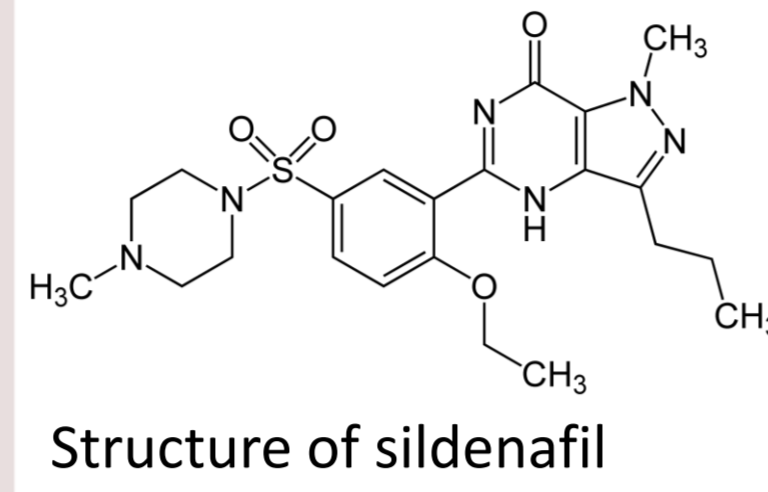
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## Introduction

### Sildenafil

- 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl]-4-methylpiperazine
- Phosphodiesterase type 5 inhibitor
- Used for treatment of pulmonary hypertension (Revatio®) and erectile dysfunction (Viagra®)



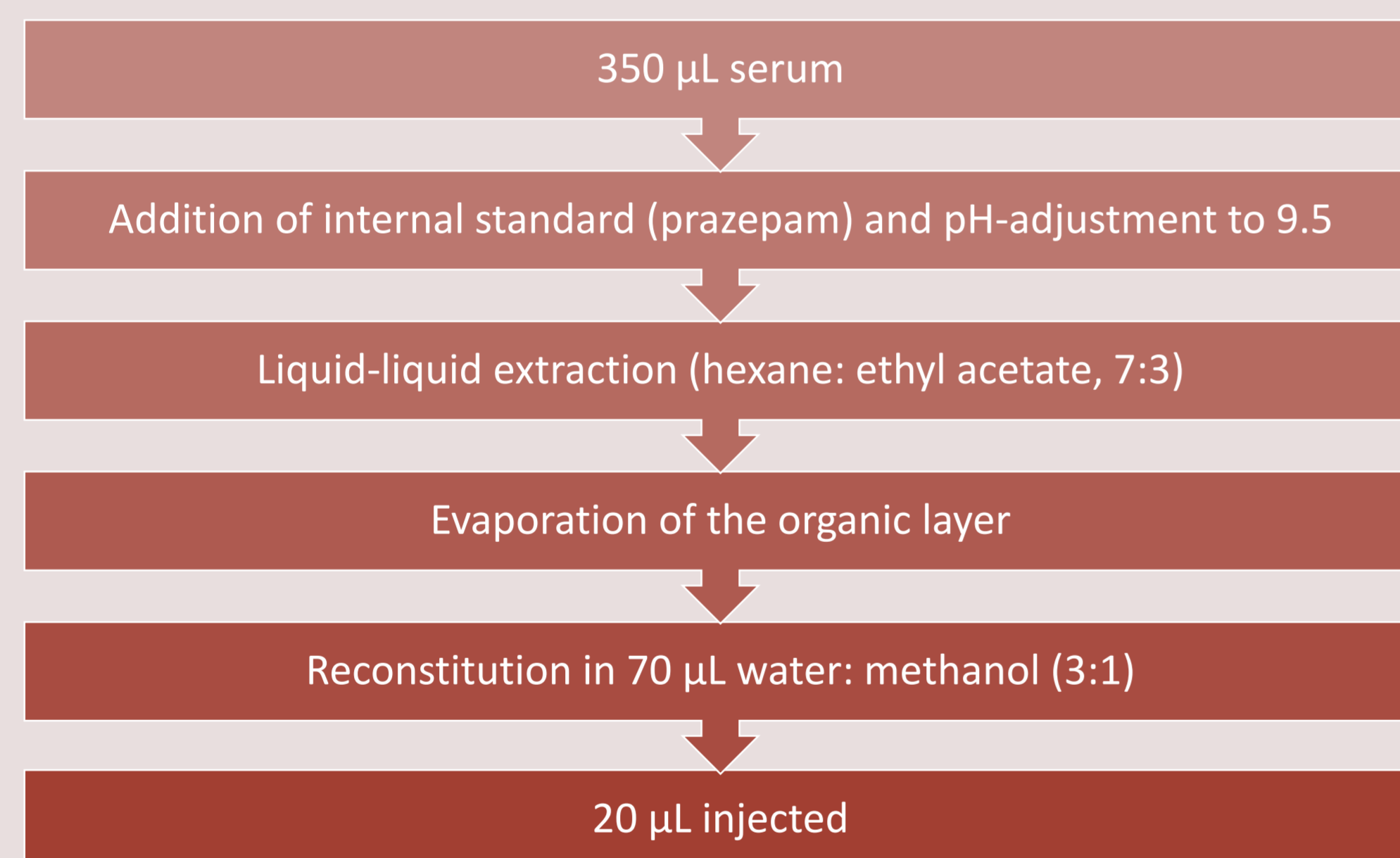
- Not generally known for its use as a self-poisoning drug
- Reports of intoxication cases have been described including some with a lethal outcome

### Case report

- 56-year-old man
- Claimed to have undertaken an unsuccessful suicide attempt by ingestion of 65 tablets of 100 mg sildenafil
- Arrived in the emergency room with severe vomiting and symptoms of blurred vision
- Sinus tachycardia of 100 bpm
- No signs of hypotension or priapism
- Supportive care was given

## Methods

Development and validation of a **high performance liquid chromatography - photodiode array** method to quantify the sildenafil level in serum



HPLC system: Agilent 1100/1200 series  
 HPLC column: Agilent ZORBAX Eclipse Plus C8, 3.0 x 150 mm, 3.5 µm particle size  
 Column temp.: 40°C  
 Gradient elution

- Solvent A: 10 mM phosphate buffer, pH 2.3
- Solvent B: 10 mM phosphate buffer pH 2.3: acetonitrile, 2:8

PDA detection at 225 nm

Time (min)	% solution A	% solution B	Flow (mL/min)
0	95	5	0.625
19	0	100	0.595
23	0	100	0.625
24	95	5	0.625
30	95	5	0.625

Chromatographic conditions

## Results

### Experimental results

- Limit of detection: 0.008 µg/mL
- Linearity: from 0.025 to 2.5 µg/mL
- 10-fold dilution integrity: 97 ± 10%

Target conc. (µg/mL)	Intra-day (n = 6)			Inter-day (n = 6)			Recovery%
	conc. (µg/mL)	CV%	% error	conc. (µg/mL)	CV%	% error	
0.025	0.029	8.3	16.5	0.025	12.9	-1.3	
0.075	0.068	7.8	-9.7	0.071	9.2	-5.8	79 ± 8
0.250	0.226	7.6	-9.8	0.240	7.7	-3.9	
2.000	1.831	10.2	-8.5	2.008	6.9	0.4	80 ± 6

Validation parameters

### Patient results

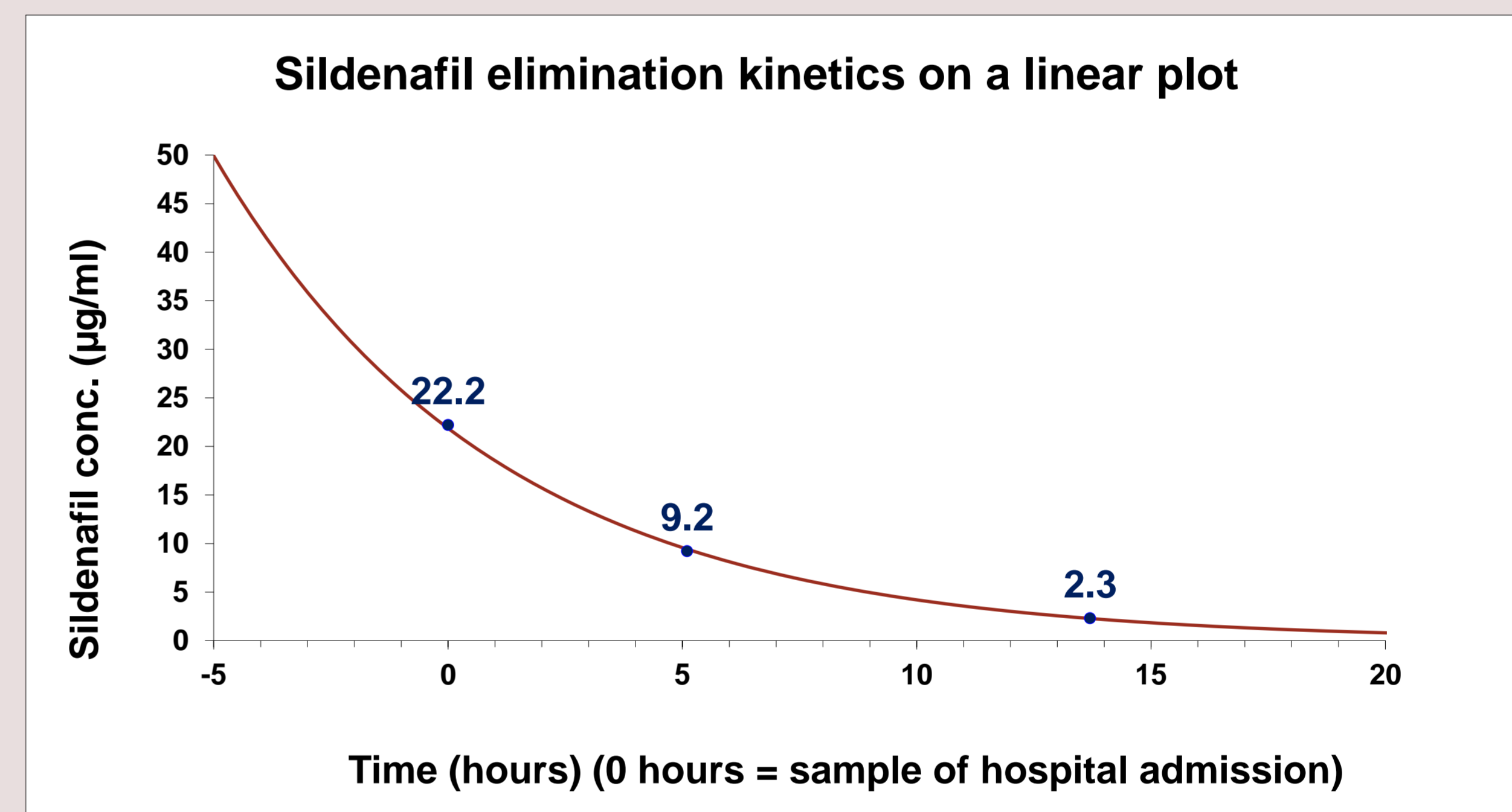
Multiple serum specimens of the patient collected over 3 days

→ Confirmation of the diagnosis of sildenafil intoxication

→ Study of sildenafil clearance

Time after hospital admission (h)	Patient serum conc. (µg/mL)
0	22.2
5	9.2
14	2.3

- First-order kinetics
- Biological half-life: ~4.2 hours



## Discussion

- Full method validation according to European Medicine Agency guidelines
- Highest reported serum conc.: 22.2 µg/mL
  - >>> Therapeutic peak conc. after a single oral dose of 100 mg: 0.5 µg/mL
  - >>> Conc. fatal case report: 6.3 µg/mL
- Half-life (4.2 h) in accordance with literature data (range: 1.4 – 4.5 h)
- Overdose pharmacokinetics similar to pharmacokinetics after therapeutic doses
- No good correlation between administered dose and clinical outcome
  - Importance of pre-existing risk factors
  - Possible drug interactions

## Conclusion

- Highest sildenafil dose ingested, resulting in the **highest serum concentration level** ever reported
- **High tolerance** in this patient: few symptoms and only moderate supportive therapy needed for recovery without sequelae
- Unofficial sale of sildenafil and variants, and exponential increase in online pharmacies remain a **major concern**, especially for patients with pre-existing comorbidities or multiple drug intake
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