

*Cisplatin meaning cis-diamminedichloroplatinum(II),  
Widely used alone and in combination to kill malignant cells,  
Testicular, ovarian, head and neck and a few more,  
The success rate in the first<sup>1</sup> being over 90% or more!*

*Since Rosenberg discovered the antitumour activity,  
The Peyrone's salt has taken up a new identity!  
But many more cancerous cells have intrinsic resistance,  
And others develop the same due to the repeated use!  
Not quite the magic bullet it has also numerous side-effects  
Including autotoxicity, neurotoxicity, nephrotoxicity, vomiting,  
Hair loss and the bone marrow suppression, limiting the dose and the use!*

*Cisplatin is highly active whilst transplatin is inactive and toxic!  
In cisplatin, Cl<sup>-</sup> and NH<sub>3</sub> are bonded to the Pt in a cis-geometry,  
While in transplatin, the same entities are linked in a trans-symmetry.  
Being more reactive, the trans-isomer is deactivated more easily,  
And being neutral, the molecules can cross the membrane readily.*

*Note that the Pt-Cl bonds are weak while the Pt-N bonds are strong,  
So that chlorides are termed as 'labile' and ammonia as the 'carrier'.  
Thus inside the cell, the halides are replaced by molecules of life<sup>2</sup>,  
And ammonias persist as carriers since the Pt-N bonds will break not.*

*The aquated dipositive ion, attracted to the polynegative DNA backbone,  
Quickly climbs up the ladder in search of the 'sweet homes'<sup>3</sup>!*

*Binding of A or G with the Pt will readily displace the aqueous moiety.  
Formation of the intrastrand Pt-1,2-GG adduct causes the DNA to bend.  
Unable to repair, unable to multiply the cell programs itself to an end!*

*Behold! The mechanisms of resistance are not fully understood,  
But may include increased repair, decreased cell uptake,  
Increased deactivation by lovers of Pt in cells called the platinophiles,  
Glutathione and metallothionein being among the wildest of the wilds!*

*Many cisplatin analogues synthesized to kill the resistant tumour cells,  
To reduce the toxic side-effects and to improve the mode of delivery,  
Examples being carboplatin, oxaliplatin, nedaplatin and ZD0473.*

*Behold! The children of Adam engaged in discoveries and invention!*

*Changing the nature of the labile groups has reduced the side-effects,  
That of the carriers has produced a limited change in the spectrum.  
Thus carboplatin has much less side-effects than parent cisplatin,  
Oxaliplatin is active in the colorectal cancer while cisplatin is not.*

*Currently research is also directed at the rule-breaker compounds<sup>4</sup>,  
Hoping that the difference in binding with DNA will alter the spectrum!*

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<sup>1</sup> testicular cancer;

<sup>2</sup> 'molecules of life' here refer to 'water molecules';

<sup>3</sup> the word 'sweet homes' refer to N7 positions of guanine and adenine;

<sup>4</sup> rule-breaker compounds are compounds that violate classical structure-activity rules such as the requirement of two labile and two carrier ligands in a cis-geometry in cisplatin analogues.