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Hyperpolarizability measurements

Many research groups in India are actively interested in nonlinear optical (NLO) materials. Novel theoretical design and synthesis of molecules with potentially large molecular hyperpolarizabilities (β) as well as crystal engineering aspects to achieve the right kind of noncentrosymmetric packing are being pursued. The critical lacuna has been the absence of indigenous experimental facilities which enable rapid measurement of second harmonic generation (SHG) coefficients and molecular hyperpolarizabilities.

The commonly used procedure is based on electric field induced SHG measurement. An alternative is now available in the form of Double Quantum Rayleigh Scattering (or Hyper Raman Scattering) experiment. P. C. Ray and P. K. Das have used the latter method (see **page 526**) to measure β for a number of weak organic acids in different solvents. The availability of data on a series of related molecules reveals an interesting trend. For a given substrate, the variation in β in different solvents parallels that of a simple thermodynamic property, viz., the pK_a of the acid in the various solvents. It is remarkable that the solvent effects on two fundamentally different molecular properties show such a linear correlation.

J.C.

Intranasal drug administration

Prolactin is a polypeptide hormone which circulates in the serum and is normally cleared by the liver and the kidney. Prolactin is secreted by the lactotrophs in the pituitary and by the decidual cells during pregnancy. The secretion of prolactin is regulated by dopamine, which inhibits the secretion of prolactin by the lactotrophs. An additional factor called the prolactin releasing factor stimulates the secretion of prolactin and may regulate normal levels of circulating prolactin. Prolactin is secreted in a sleep-related, circadian manner with highest levels observed shortly after the onset of sleep. Normal circulatory levels of prolactin are around 20 ng/ml, but during pregnancy, can reach levels as high as 200 ng/ml. Prolactin has both mammogenic and lactogenic action in humans.

Hyperprolactinaemia is characterized by elevated levels of prolactin which can reach 100 ng/ml in some cases. The causes of hyperprolactinaemia could be due to the presence of pituitary adenomas in both men and women; certain drugs such as anesthetics, oral steroid contraceptives and antihypertensive drugs such as α-methyldopa can cause hyperprolactinaemia by interfering with the production of dopamine. In certain cases, hypothyroidism can also lead to hyperprolactinaemia by the overstimulation of lactotrophs. In women, elevated levels of prolactin can lead to galactorrhea or watery or milky secretion from the breast, and frequently amenorrhea or the cessation of normal menstruation. Mechanisms are poorly understood, but it is believed that prolactin increases dopamine turnover, resulting in reduced norepinephrine levels which, in turn, affect the secretion of gonadotrophins which control the menstrual cycle. Such menstrual abnormalities lead to reduced fertility. In men, hyperprolactinaemia leads to reduced libido and causes impotence.

The main treatment for hyperprolactinaemia should result in the elimination of lactation and the induction of ovulation in women. This is usually achieved by the administration of bromocriptine, which is a potent dopamine agonist. Administration of 5 mg/day bromocriptine significantly reduces prolactin levels during the course of treatment, and restores menstrual cyclicity in 10–16 weeks. However, a number of side effects have been reported in patients being administered bromocriptine, such as nausea, headaches and dizzyness and this has necessarily curtailed its use. A recent report has shown that vaginal administration of lower doses of bromocriptine could achieve a reduction in circulating prolactin levels, without adverse side effects. In the paper by Suresh *et al.* in this issue (**page 528**) intranasal administration of bromocriptine has been attempted in a small number of hyperprolactinaemic patients, in an effort to provide an alternative route of administration of bromocriptine, in lower doses with consequent reduced side effects.

Intranasal administration of drugs is the method of choice for the administration of a number of drugs used as therapy for respiratory diseases. Nasal administration of pharmacologically active drugs and steroids was pioneered in the seventies by Dr T. C. Anand Kumar at the All India Institute of Medical Sciences, New Delhi. He and Prof. N. R. Moudgal have shown earlier that intranasal administration of microdoses of steroids/drugs is effective in acting at the hypothalamo-pituitary axis, bypassing systemic circulation, and can therefore regulate hormone release. What is significant in this paper is the evidence that low doses of bromocriptine administered intranasally can achieve a reduction of circulating prolactin levels within three weeks, with no side effects reported by the patients tested. The only reported discomfort was irritation during inhalation of the spray, but a modification of the solvent used in the spray could alleviate these effects as well. Certain patients still required high (2 mg/ml) doses but interestingly, they did not report any nausea or vomitting. Further studies are required with a larger number of patients but the results are encouraging, and it is hoped that this methodology can be commercially exploited by drug manufacturing companies in this country to enable doctors to adapt this line of treatment in future.

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