

illustrated. This chapter is peppered with amazing nuggets of information. For example, it describes the meticulous record kept by Jehangir of his hunting 28,352 animals over a 38-year period, the first record of cheetahs breeding in captivity in 1613, the game hunts in the Palam area of Delhi in 1619 where the airport stands today, the areas earmarked within the empire for cheetah procurement, and so on. The Mughal paintings reproduced as colour plates offer the reader a glimpse of the era and the spectacular sport of coursing.

The purpose of any historical sketch should be not so much to accurately describe as to incisively examine cause and consequence, to tease apart cultural and political, psychological and ecological processes that created the historical events. The present book offers excellent descriptions and analyses of historical events pertaining to the cheetah, and opens up new arenas for more incisive analyses of the factors leading to its decline and eventual extinction. What was the intensity of procurement of cheetahs from the demarcated areas of the empire and how did it affect their populations? Akbar, according to the *Iqbalnama*, is reputed to have procured over 9000 cheetahs. Jehangir recounts that Akbar had 1000 cheetahs in his menagerie. How credible could these claims possibly be and what happened to the animals in the royal menagerie with the fall of the Mughal empire? Was the low breeding potential of cheetahs a significant factor in their decline or was it dominated by other forces? How were the historical changes in human populations, cultures, kingdoms, agricultural practices, and hunting linked to the creation or destruction of open habitats and prey base of cheetahs?

With the rise of British dominion, the peculiar cultural association between humans and cheetahs waned, as did the wild populations of cheetahs. In Chapter 5, the author makes a not entirely convincing case that the cheetah was not a major item on the *shikar* agenda of the British, who also did not take to the sport of coursing as it was too 'passive' for them. Recent analysis of archival records (in a forthcoming paper by Mahesh Rangarajan) of bounties paid for killing cheetahs indicates that the role of the British in the extermination of cheetahs may not have been entirely

'inadvertent'. Another conclusion derived by the author from records of the British period is, however, particularly insightful. With shrinking habitats, hunting, and an increasing scarcity of wild prey, the cheetahs were forced into sub-optimal habitats (even dense jungle) and began to prey on village livestock. This feature, common even today for many endangered species, highlights a point that conservationists cannot afford to forget. Existing refuges for endangered species may not always contain the best habitats for them. Instead, they may only represent areas most sheltered from the inimical forces causing their endangerment.

After an inevitably brief chapter on the cheetah in independent India, there is a fascinating chapter on the trapping, training, handling, and coursing of cheetahs that will be of particular interest to technicians in modern zoos and historians. The two succeeding chapters are about African cheetahs brought into Asia and the taxonomic status of African and Asian cheetahs. The author points out that the minor sub-specific differentiation of African and Asian cheetahs (chiefly in the tail tip being black in the Asian race vs white in the African) is more a result of 'historical observation rather than of any taxonomic study'. Chapter 10 presents a depressing and eye-opening review of the status of the cheetah in Asia, where the species has virtually disappeared from all countries except Iran, where some 50 to 200 individuals may survive. Highlighting that the need to protect it there is paramount, the author says 'how many will be available for reintroduction in India is another matter'.

The last chapter, which is perhaps the most important one from the standpoint of the stated purpose of the book, is one of the shortest (four pages). The analysis of the causes of decline and extinction of cheetahs, some of which is in earlier chapters and some in Appendix F (Chronology of Extinction) could have been comprehensively compiled and addressed here. A direct comparison with the other large carnivores, the lion and wolf, which are highly endangered today, would have been valuable in evaluating the relative importance of different causative factors in triggering the extinction of cheetahs. Of particular interest to conservationists would be the

plan to reintroduce cheetahs in India, formulated by M. K. Ranjitsinh, and described by the author. The given outline of the plan is clearly sketchy and preliminary but deserves serious consideration and further study. As a prerequisite, however, it is necessary to objectively assess the feasibility and desirability of reintroduction. One must learn from earlier successes as well as avoid past mistakes (such as lack of scientific monitoring and planning, and working with inadequate knowledge of the species' ecological requirements) which led to failures of projects such as the lion reintroduction in Chandraprabha in 1957.

With worldwide concern today over preventing extinctions and conserving natural ecosystems, the content of the book is timely and relevant. Its multidisciplinary nature makes it a useful reference for historians, wildlife enthusiasts, ecologists, conservationists, managers, and policy makers. There are only a few minor typographical and stylistic errors, including misspelling of scientific names of some species (for instance, the blackbuck *Antelope cervicapra*). The elegant format of the book, with the large number of plates and illustrations, make the book as attractive as it is informative. Anyone who buys this book is unlikely to regret it.

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Venom Phospholipase A₂ Enzymes: Structure, Function and Mechanism.
R. Manjunatha Kini, ed. John Wiley and Sons. 1997. 511 pp. Price: US\$70.

Phospholipases are classified according to the position of the bond which they hydrolyse in a phospholipid molecule. Thus, we have phospholipases A₁ which are widely distributed in nature and hydrolyse sn-1 position in the phospholipid. Phospholipases A₂ are ubiquitous in nature; attack 'phospholipids at the sn-2 position of the glycerol backbone, releasing lysophospholipids and fatty

acids. They hydrolyse various naturally-occurring phospholipids such as phosphatidylcholine, phosphatidyl ethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, plasmalogen, plasmenylcholine, platelet aggregation factor and 1-alkylether-phosphatidylcholine' (pg. 1). Phospholipase C, generally associated with secretions of certain pathological bacteria, also occurs in plant tissues and hydrolyses the phosphodiester bond liberating the phosphorylated base. Phospholipase D is most well studied in plants although its presence in other sources such as mammalian tissues is also known. It also attacks the phosphodiester bond and liberates the base. In addition, there are minor enzymes which also hydrolyse phospholipids. For example, phospholipase B (which hydrolyses bonds at both sn-1 and sn-2 positions). It should also be added that not all phospholipid hydrolysis is catalysed by phospholipases. Some triacylglycerol lipases have been reported and acyl hydrolases, particularly in plant leaves are known to be active towards phosphoglycerides.

The present multi-authored book is a collection of 18 chapters devoted to various aspects of phospholipase A₂. Further, as made clear in the title, while the enzyme is ubiquitous, the focus in this book is exclusively on the enzymes from snake venom. The subtitle reads as: Structure, function and mechanism which may lead one to expect greater emphasis on the biochemical and bio-organic chemistry of the enzyme, this is not so. In fact, larger portion of the book is devoted to pharmacological aspects. This is not unreasonable when one is talking about enzyme from snake venom. The phospholipases, in general (unlike general esterases), function on interfaces. These enzymes have low activity against monomeric soluble phospholipids but show a sudden increase in activity as the substrate phospholipid concentration reaches the critical micelle concentration. Hence, the interfacial catalysis may involve 'hopping mode' or the 'scooting mode' depending upon whether the enzyme does not or does remain bound to the interface at the end of each catalytic turnover cycle.

Phospholipase A₂ enzymes can be both intracellular or extracellular/

secretory. The latter class includes snake venom enzymes and has relatively low molecular weight in the range of 13,000–15,000. They all require Ca²⁺ for their catalytic activity. The primary sequence of more than 150 enzymes belonging to this class is known and based upon this, the four different groups of enzymes have been defined. These cysteine-rich proteins contain between 119 and 134 amino acid residues, showing large proportion of invariant residues which are either involved in catalysis or are important for native structure. The histidine residue at position 48 is conserved in these enzymes and is an active site residue. Quite a few enzymes, e.g. from human synovial fluid and venom glands of *Naja naja* and *Apis mellifera* have been cloned and overexpressed.

'Catalysis can be conceptually divided into four phases, binding of Ca²⁺ cofactor and substrate, general base mediated attack on the productively bound substrate, formation and collapse of the tetrahedral intermediate and product release' (p. 112). Ca²⁺ plays multiple roles in these secretory phospholipases. It directs the stereospecific positioning of substrate in the active site of the enzyme, serves as an electrophile and polarizes the sessile ester bond, stabilizes the transition state and 'also strengthens the electrostatics underlying interfacial absorption' (p. 114). A second coordinated Ca²⁺ has also been observed in several high resolution crystal structures and is believed to function as an additional electrophile.

The first chapter authored by the editor himself provides a good overview of the book or (for that matter) of the various aspects of phospholipase A₂. Not much is mentioned about purification strategies here or in later chapters. Snake venom phospholipase A₂ often contains a large number of isozymes. An interesting observation in the second chapter (dealing with cloning and analysis of cDNAs and genes encoding venom phospholipase A₂) is: 'It is now clear that the functional diversity of toxins is associated with a structural economy. In other words, a small number of structural scaffolds have been selected by venomous animals to exert numerous different functions.' Thus, one can talk of phospholipase A₂

(PLA₂) fold associated with the expression of toxicity of snake venoms. The third chapter continues with the characterization of genomic clones and looking at the structural organization of the genes. There is quite a lot of overlap with the earlier chapter and some avoidable repetition. The fourth chapter looks at secondary, tertiary and quaternary structures of these enzymes and briefly talks about the catalytic mechanism. The importance of various residues for the interfacial adsorption, as obtained from chemical modification and mutational studies is also discussed.

Rosenberg has written two extremely readable and interesting chapters (Chapters 5 and 6) on the correlation between enzymatic activity, lethal doses and pharmacological properties of snake venom phospholipase A₂. 'The enzymes in snake venom, with the exception of PLA₂, are generally of low toxicity and have not been implicated as the major lethal factors of snake venoms. In contrast, PLA₂ enzymes vary dramatically in their lethal and pharmacological potencies, from those with low lethality and no specificity of action to those which are so toxic and so specific in their actions that we no longer call them PLA₂ enzymes, but call them PLA₂ toxins or neurotoxins.' Thus, we have *Naja naja atra* PLA₂ with LD₅₀ > 1 mg/kg with high enzymatic activity and no organ specific action and β-bungarotoxin with low enzymatic activity but presynaptically acting toxin as examples from two ends of the spectrum. Apart from raising ethical concerns about use of animals in determination of LD₅₀ values and a very good discussion on valid methods for determining these values, the author has also provided a very balanced overview of possible mechanisms of PLA₂-induced lethality and possible correlation between LD₅₀ values and enzymatic activities of PLA₂ enzymes and toxins. He also points out that the question – Is enzymatic activity essential for lethal potency? – is a difficult one to answer. A rather extensive set of experimental data is provided to justify the conclusion that the relationship between enzymatic and pharmacological activities cannot be generalized.

Another chapter (Chapter 8) which may be of more general interest is on

compounds of plant origin which may be used as remedies of snake bites. The studies described here on interaction of alkaloids like aristolochic acid with phospholipase A₂ from *Vipera russelli* and *Trimeresurus flavoviridis* venoms at molecular level are obviously a prelude to providing rational basis for use of some folk medicines. More important, the scientific framework for this approach needs to be developed so that these plant isolates become a powerful alternative to antivenin therapy. The chapter by Stiles and Choumet (Chapter 9) reviews the antivenin therapy based upon monoclonal antibodies raised against phospholipase A₂ and the toxins. The next two chapters talk about the structural data and structure-function relationship work with monomeric and multimeric neurotoxins. In the latter, at least one of the subunits has phospholipase A₂ activity. Some snake venoms result in local myotoxicity (degeneration of muscle around the site of injection) whereas others act as general myotoxins (affecting widespread muscle groups). The last chapter in the book later on suggests that acylation of specific membrane-bound proteins could be a likely mechanism of myotoxicity. The two successive chapters (Chapters 12 and 13) provide the general picture about myotoxicity of phospholipase A₂ enzymes and that resulting from Bothrops snake venoms in particular respectively. The anticoagulant effect of these enzymes and their effect on platelet aggregation is adequately treated in Chapters 14 and 15. Identification of membrane receptors for the enzymes and the cellular effects of presynaptically acting phospholipases are covered in Chapters 16 and 17.

Thus, there is greater emphasis in the book on phospholipases which act as toxins rather than the less toxic enzymes. An extensive coverage of phospholipase A₂ makes this a rather valuable book for anybody working with this particular class of enzymes. Obviously, because of its rather narrow focus, this may not interest a general biochemist.

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The Legacy of Galileo

Galileo, Newton, Halley and Einstein in 90 Minutes. John and Mary Gribbin, Universities Press, 3-5-819, Hyderguda, Hyderabad 500 029. Price: Rs 45 each.

Some individuals, through their extraordinary contributions, etch their names on the canvas of time and become immortal. Galileo, Newton and Einstein are in this select club. Hence, it is always tempting to read and write about them. John and Mary Gribbin could not resist the itch to write about these great men. Instead of summarizing the contents of these little biographies, I will dwell upon some of the pieces that are not generally emphasized in popular biographies of these men.

Galileo was the first to stress the importance of experimentation as exemplified by his own experiments. In this context we refer to an interesting anecdote described by Gribbins. A Professor at Pisa, dropped two bodies of different weights from the Leaning Tower of Pisa and 'gleefully pointed out that they failed to hit the ground *exactly* at the same time' as claimed by Galileo. Galileo while responding to his critics correctly attributed this to an error in the experiment. He was the first to point out the possibilities of errors in an experiment and their proper evaluation.

The book has a vivid description of the society of those times. Galileo's father had promised a substantial dowry to Galileo's sister. Galileo had not only to meet this financial obligation but also had to give dowry to his second sister. He could not meet these commitments in his entire life and to add insult to injury, his brothers-in-law sued him in a court for not settling their dowries. This left such a scar on him that he forced his two daughters, whom he loved very dearly, to be nuns for life.

The authors bring out the interesting fact that Leonard Digges had built a refracting telescope way back in 1550. But Galileo went beyond constructing a telescope. He established on a sound footing the Heliocentric theory. Gribbins point out that Galileo attributed the eternal circular motions of planets round the Sun to a Principle of Inertia according to which bodies on their own always move in circles. It was Rene Descarte who realized that this concept

of inertia applied only to motions in a straight line. But it was left to Newton to analyse motion in a curve.

This brings us to the book on Newton. If we do not believe the 'apple story', it is difficult to speculate on what made Newton to invent the Law of Gravitation. Gribbins argue out that that was a natural sequel to his discovery of the centrifugal force acting on a particle moving on a curve. A planet in an orbit would be driven away from the Sun by the centrifugal force. In order to keep it in its orbit there must be an equal and opposite force tugging it towards the Sun. Using Kepler's Law about orbital periods Newton discovered that this force of attraction should fall inversely as the distance from the Sun. Thus was born his Universal Law of Gravitational attraction.

We all know that Newton became a Fellow of the Royal Society of London for his invention of the reflecting telescope. The authors rightly give credit again to Leonard Digges for being the first to make such a telescope. Gribbins also highlight an interesting event in Newton's life. Within a few years after becoming the King of England, James II, a catholic, ordered that a Benedictine monk Francis be conferred the MA degree by the Protestant dominated Cambridge University. Newton then, an unknown personality, risked his life by openly criticising the King and was mainly responsible for the University's refusal to award the MA degree to Francis. He and the other Cambridge Fellows were asked to explain their conduct to one Lord Chancellor, Judge Jeffreys who in the previous year had got 300 people hanged for opposing the King.

Undoubtedly Galileo and Newton are household names. Halley, by contrast, is remembered only when a comet appears in the sky. Thus his biography is very welcome. Many unknown facets of this colourful personality have been brought out by these authors. Halley was born rich and had the full support of his father in his scientific pursuits. When he was just 20 years old, his father financially backed his sea voyage from St. Helena to South Atlantic. His study of the southern sky during this tour led to his well known book *Catalogue of the Southern Stars*. For this work he was elected a Fellow of the Royal Society of London. He became financially broke