Possibility of auto-inoculation of blood for tick control in cattle

Ticks (Acarina: Ixodidae) are important blood-sucking arthropod parasites of livestock which cause great discomfort to them, besides their vital role in transmission of deadly protozoan and rickettsial diseases. The concept of treating warts or infectious papillomas in cattle by autogenous vaccine was our aim while initiating a preliminary attempt of auto-inoculation of blood to tick-infested calves to know its possibility in tick control.

Eleven infested crossbred male calves, 10–24 months old, with natural infestation of all developmental stages of ticks, mainly of *Boophilus annulatus* followed by *Rhipicephalus* sp., were selected for the study. Seven calves were selected as experimental and four as control. Ticks on the entire body of these calves were counted once in seven days for 21 days of the observation period. The required quantity of fresh blood was directly drawn from the jugular vein using sterilized syringes and needles. The collected blood was immediately inoculated at a dosage rate of 1 ml per 10 kg body wt intramuscularly (i/m) to thigh muscle to five calves (group 1) and subcutaneously (s/c) to the neck region to two calves (group 2). One of the calves of the former group was given a booster dose on day 7. Three calves were kept as control for group 1 and one calf for group 2. All the inoculated and control calves were allowed to graze for 7–8 h with the rest of the infested herd, exposing them to equal and uniform chances for tick infestation. The percentage of efficacy of auto-inoculation in reducing tick infestations was calculated using the formula: $[1 - (T_2/T_1) \times (C_1/C_2)] \times 100$, where T_1 is pre- and T_2 post-inoculation means of tick count, while C_1 and C_2 are the corresponding means of control.

Reduction in the number of ticks was observed from the first week of inoculation in both treated groups. The mean reduction of 63.93% of ticks was noticed on day 21 in four calves that had single i/m inoculation. The calf which received the booster dose by i/m route and those that had single s/c inoculation showed 73.99 and 74.12% reduction respectively, on day 21, indicating a higher percentage of reduction of ticks compared to calves that had single i/m inoculation. Ticks appeared pale or bluish, small in size, and the fully engorged ones were rarely seen.

The morphological changes of ticks and the reduction in their numbers noted in the present study may have been influenced by immunological reactions. Usually sufficient salivary secretion of ticks entered the circulation of the infested hosts from the site of bite and initiated antigen–antibody reactions producing partial immunity[1]. But the antibodies developed were inactive or non-protective in nature, as evidenced by the common occurrence of continuous building up of tick infestation in animals. The transfer of circulating blood containing these antibodies to their muscular or subcutaneous tissues as done in our experiments probably triggered the immune system to the possible extent, which was reflected in terms of the number of ticks rejected from the host. A recent report[2] on the operation of an immunologic effector mechanism auto-vaccination for bacterial infection in cattle[2] supports this view. The activation of silent antigen–antibody complex leading to early dropping, discolouration and size variation of ticks as reported in immunized animals with tick extracts[3,4], was also noticed in the present study. Since the present study with limited number of calves is purely an initial attempt, further investigations are required to substantiate the views put forward.

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US Patents granted to Indian pharmaceutical companies

The debate around patents is mostly related to pharmaceutical products. The pharmaceutical industry globally is pushing hard for recognition of patents for pharmaceutical products even in developing and least developed countries. The Trade Related Aspects of Intellectual Property Rights (TRIPS) is an instrument through which patents are enforced. The main reason cited for recognition of patents related to pharmaceutical products is the cost of drug discovery and development. Lag time from the identification of potential drug molecules to their successful marketing is around 12–15 years and is expensive (around 1 billion USD), according to various sources. India became a member of the WTO (World Trade Organization) and agreed to abide by the TRIPS agreement. India had 10 years time for shifting from regime of process patent to product patent. Pharmaceutical companies in India were reluctant to accept product patents as the Indian Patents Act 1970 helped these domestic pharma companies to achieve growth and be regarded as quality suppliers of generic

Table 1. Patents granted to Indian pharmaceutical companies by USPTO

Institution	Pre-1995 patents	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	Total
CSIR	47	9	10	18	25	36	37	58	120	133	127	117	122	859
Ranbaxy Laboratories Limited	7	1	1	2	5	4	4	8	7	8	11	7	12	77
Dr Reddy's Research Foundation	0	0	0	1	2	7	7	3	7	1	0	0	2	30
Dabur Research Foundation	0	0	0	0	0	1	3	5	5	6	1	2	3	26
Panacea Biotec Limited Pharmaceuticals Ltd	0	0	0	1	1	4	2	3	2	1	0	NA	NA	14
Orchid Chemicals and	0	0	0	0	0	0	0	0	2	5	6	5	1	19
Lupin Laboratories Limited	0	0	1	1	5	2	1	1	0	0	0	NA	NA	11
Dr Reddy's Laboratories Ltd	0	0	0	0	0	0	0	0	0	7	3	5	7	22
Torrent Pharmaceuticals Ltd	0	0	0	0	0	0	1	3	1	3	0	0	1	9
USV Limited	0	0	1	0	0	0	0	1	2	1	2	1	0	8
Biocon India Limited	0	0	0	0	0	0	0	1	0	4	1	4	0	10
Department of Science and Technology	0	0	0	0	0	0	0	0	3	1	2	0	0	6
Aurobindo Pharma Limited	0	0	0	0	0	0	0	0	2	0	3	1	3	9
Wockhardt Limited	0	0	0	0	0	0	0	0	0	3	2	2	4	11
Sun Pharmaceutical Industries Ltd	NA	NA	NA	NA	NA	NA	NA	NA	2	2	0	1	4	9

NA, Not available.

drugs. Though adamant, Indian pharma companies started gearing up for product patent regime. This is evident from the data (Table 1) from USPTO (United States Patents and Trademarks Office)[1,2] which show patents filed by Indian pharma companies in the United States. It is interesting to note that prior to 1995, except Ranbaxy Laboratories Ltd, majority of Indian pharma companies did not have US patents. Even after 1995, the performance of these companies in acquiring US patents was abysmal. Majority of the pharma companies got patents after 2000. This may be attributed to the fact that the process of acquiring patents takes a few years. One of the plausible reasons could be filing of patents immediately after India adhered to the TRIPS agreement. These companies thought of the inevitable and prepared themselves to face challenges imposed by TRIPS. Among the pharma companies, Ranbaxy Laboratories Ltd is the frontrunner in acquiring US patents, with 77 patents to its credit from 1969 to 2006. Dr Reddy's comes a close second, with 52 US patents from 1995 to 2006 (Patents for Dr Reddy's Research Foundation (30 patents) and Dr Reddy's Laboratories Ltd (22 patents) combined together). The other major pharmaceutical companies have less than 20 patents each. This can be seen in Table 1. It is not known whether these patents are process or product patents, as further classification is not provided by USPTO. It is also not known as to how many of these patents have been filed through the PCT (Patent Cooperation Treaty) route. But information provided by Ranbaxy Laboratories Ltd to the Mashelkar Committee suggests that patents have been obtained in the US primarily for generics[3]. This could be attributed to the fact that Indian companies have established their strong base on 'reverse engineering' skills and capabilities in producing quality generic medicines. Due to the high cost of R&D associated with drug discovery, Indian companies have taken a relatively safer path of developing and marketing generic medicines. It is commendable that Indian pharmaceutical companies have accepted the challenges posed by the TRIPS agreement, and are investing in R&D and acquiring patents in the US.

1. Company and year patent data obtained from, www.uspto.gov/web/offices/ac/ido/oeip/taf/asgstca/inx_stc.htm, accessed on 19 December 2005 (data from 1969 to 2004).
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