Pharmacokinetic study of 11-Keto β-Boswellic Acid

S. Sharma¹, V. Thawani², L. Hingorani³, M. Shrivastava⁴, V. R. Bhaté⁵ and R. Khiyani⁶

¹Pharmacology, Indira Gandhi Medical College, Nagpur, India
²Pharmacology, Government Medical College, Nagpur, India.
³Pharmanza (India), Kansari, India
⁴Department of Pharmacology, Indira Gandhi Medical College, Nagpur, India
⁵Indtech Analytical, Ansa Industrial Estate, Mumbai, India
⁶Government Ayurvedic College, Nagpur, India

Summary

Introduction: *Boswellia serrata* has been used in traditional medicine for treatment of inflammatory diseases since antiquity. However human kinetic studies are lacking for this. Hence to better elucidate its effects in humans and determine its optimal dosing, this study was planned. Material and Methods: Twelve healthy adult men volunteers were given capsule Wok Vel™ containing 333 mg of Boswellia Serrata Extract, orally, after a seven days washout period. Venous blood samples were drawn through indwelling canula from each volunteer prior to drug administration and at 30, 60, 120, 150, 180, 210, 240, 300, 360, 480, 600, 720, 840 minutes after drug administration. Plasma obtained after centrifuge was analyzed to measure concentration of 11-Keto β-Boswellic Acid (KBA) by HPLC. Various kinetic parameters were then calculated from the plasma concentrations.

Results: The results are expressed as mean ± Standard Error of Mean. The peak plasma levels (2.72 × 10⁻³ ± 0.18 µmoles/ml) of BSE were reached at 4.5 ± 0.55 h. The concentration declined with a mean elimination half life of 5.97 ± 0.95 h. The apparent volume of distribution averaged 142.87 ± 22.78 L and the plasma clearance was 296.10 ± 24.09 ml/min. The AUC 0–∞ was 27.33 × 10⁻³ ± 1.99 µmoles/ml h.

Conclusion: Elimination half life of nearly six hours suggests that the drug needs to be given orally at the interval of six hours. The plasma concentration will attain the steady state after approximately 30 hours. BSE is a safe drug and well tolerated on oral administration. No adverse effects were seen with this drug when administered as single dose in 333 mg.

Key words: *Boswellia serrata*, pharmacokinetic

Introduction

Traditional medicine from all the ancient civilizations has come upfront during the last decade, throughout the world as pressing need for the alternatives is mounting. The richness and diversities of these drugs are indeed appealing, enchanting and enticing. In India, Ayurveda has been practiced for ages. There is some overlap in the herbal and Ayurvedic medicines. Effort is on to provide the scientific validity to these medicines by applying the methodology of modern medicine. Many herbal drugs are used without the sub-
stintitative kinetic data. This study is one such attempt to validate the usage of an ancient drug.

*Boswellia serrata*, known as Gajabhakshya in Sanskrit, implying its ingestion by elephants has been used in the Ayurvedic medicine since antiquity. The interest in this herb was aroused by the fact that such a heavy animal carried its weight on its limbs for so long, yet lived longer than humans (Selected medicinal plants of India, 1992). This stimulated effort to find the ingredients in its diet, where Boswellia was found to be one. Boswellia has been mentioned in the ancient Indian Ayurvedic texts – the Sushruta Samhita and Charak Samhita (Kulkarni et al. 1991; Alternative Medicine Review 1998). Boswellia is a tree of moderate height, which grows widely on dry hills of northwest India. In Ayurveda the oleogum resin of BSE is known as ‘Salai Guggul’ or ‘Sallaki Guggul’. It has been used in the treatment of rheumatism, nervous diseases and as a topical anti-inflammatory agent.

Preparations from the gum of Boswellia Serrata Extract (BSE) have been used in traditional/folk medicine for treatment of inflammatory diseases. On stripping the bark, it yields gummy oleoresins, which contain oils, terpenoids and gums. Upto 16% of the resin is essential oil, the majority being α thujene and p-cymene. Four pentacyclic triterpene acids are also present, with β-boswellic acid being the major constituent (Chatterjee and Pal, 1984; Kirtikar and Basu 1935).

BSE showed anti-inflammatory and antibacterial activity while the non-phenolic fraction of gum resin exhibited sedative and analgesic effects when tested in rats (Alternative Medicine Review, 1998). Animal and in vitro studies suggest its usefulness in many inflammatory and broncho-constrictive conditions. Animal studies performed in India show that ingestion of defatted alcoholic extract of BSE decreases polymorpho-nuclear leucocyte infiltration and migration, decreased antibody synthesis and caused almost total inhibition of the classical complement pathway. Recently, it has been shown to be the inhibitor of 5-lipoxygenase and also human leucocyte elastase (Safayhi et al. 2000; 1997; 1992) and consequently it has been proposed in the treatment of various inflammatory conditions (Gupta et al. 1997).

In 1992, the active principles within the multi-component mixture of resin were identified, resulting in recognition of Boswellic acids. The most important are Acetyl 11-Keto β-Boswellic Acid (AKBA) and 11-Keto β-Boswellic Acid (KBA).

The therapeutic importance of this drug is reflected in the current efforts to characterize the biopharmaceutical parameters. Besides various experimental investigations, different clinical data from patient treatment and several studies has been published. However human kinetic studies are lacking for this substance, and therefore need to be conducted to better elucidate its effects in humans, as well as to determine optimal dosing. Published kinetic studies on BSE are rare. (Pubmed Search).

Pharmacokinetic study is necessary to understand the time course of a drug and its effect in the human body. Kinetic data used to determine the optimum dose, establish dosing schedule, provide a baseline when treatment in disease is initiated, correlate plasma concentration at which beneficial effects are observed, monitor the course of patients experiencing adverse drug reactions and overdose.

The present study was planned to detect the more pronounced inhibitors of 5 Lipo-oxygenase AKBA and KBA in human plasma.

### Material and Methods

#### Design

This was an oral single dose, open, uncontrolled pharmacokinetic trial on 12 healthy men volunteers, with a one week pre-drug wash out period. The study was carried out at the Clinical Pharmacological Unit (CPU) in the Department of Pharmacology, Indira Gandhi Medical College, Nagpur, India. The study was approved by the Institutional Ethics Committee and performed according to the principles of the Helsinki Declaration.

#### Drug

Drug Wok Vel™ containing 333 mg of Boswellia Serrata Extract was supplied by Pharmanza (India). Each capsule of Wok Vel™ contained the standardized BSE gum with a minimum of 65% organic acids or minimum 40% total Boswellic acids (BA). Main components of boswellic acid in BSE used were 11-keto-β BA (KBA) – 6.44%, 3-O-Acetyl-11-keto-β BA (AKBA) – 2%, β-BA – 18.51%, 3-O-Acetylb-β BA – 8.58%, α BA – 6.93% and 3-O- Acetyl-α BA – 1.853%.

#### Subjects

Healthy men volunteers between 18 to 50 years of age, free from significant, physical or psychiatric disorders as determined by medical history, physical examination, clinical chemistry, hematology and urine analysis were included for the study. Volunteers were excluded from the study if they had any significant abnormal test results or had received any drug treatment during past three months. They were also excluded if they had any history suggestive of allergy or blood donation in last one month. Volunteers gave written, witnessed and informed consent in vernacular language prior to partici-
Kinetic study of 11-Keto β-Boswellic Acid

Participants were monitored for adverse reactions, if any, with special attention to epigastric pain, nausea, vomiting and diarrhea.

Study protocol

On the day of the trial, volunteers reported in CPU at 0800 hrs. After briefing, documentation and acclimatization a standardized breakfast was given. Then, an indwelling venous catheter (Vasofix no. 20) was fixed in the forearm using all aseptic precautions. One capsule of BSE was then administered orally with 100 ml of water, under supervision. Volunteers remained inside the CPU till the last blood sample was taken and during this time they received same meals. Concomitant medication, tobacco or other intoxicants were not permitted during the study. Venous blood samples (5 ml each) were drawn from each volunteer prior to drug administration and at 30, 60, 120, 180, 210, 240, 300, 360, 480, 600, 720 and 840 minutes after drug administration. Blood samples were collected in EDTA Vacutainer™ and were centrifuged (1500 rpm for 20 minutes) immediately to separate plasma. The collected plasma was refrigerated till analysis. The concentration of KBA and AKBA in plasma was determined by HPLC.

Analytical Procedure (Krohn et al. 2001; Kaunzinger et al. 2002)

- **Step 1 – Extraction**: One ml of plasma was taken in a stoppered conical test tube and 1 ml of 0.1N HCl was added, and vortex for 1 minute. 5 ml of Diethyl Ether-n-Hexane (2:1, v/v) was added and vortex for 1 minute. 5 ml of Diethyl Ether-stoppered conical test tube and 1 ml of 0.1N HCl was added, and vortex for 1 minute. 5 ml of Diethyl Ether-stoppered conical test tube and 1 ml of 0.1N HCl was added, and vortex for 1 minute. 5 ml of Diethyl Ether-stoppered conical test tube and 1 ml of 0.1N HCl was added, and vortex for 1 minute. 5 ml of Diethyl Ether-stoppered conical test tube and 1 ml of 0.1N HCl was added, and vortex for 1 minute.

  Upper organic layer was transferred in a marked test tube, and the organic layer evaporated to dryness at 40 degrees centigrade using nitrogen stream. 250 ml of reconstituent (70% aqueous methanol adjusted to pH 10.7 with liquor ammonia) was added, vortex for 30 seconds and centrifuged at 3000 RPM for 1 minute.

  1 milliliter of n-Hexane was added and vortex for 30 seconds, centrifuged at 3000 RPM for 1 minute and lower layer analyzed by HPLC.

- **Step 2 – Operational conditions**: HPLC analysis was carried out using hypersil-C-18 column 5 mm ODS (250 × 4.6 mm), employing mobile phase constituting acetonitrile:methanol:0.6% acetic acid (73:10:17, v/v) pH 3.0 in isocratic elution mode and detection by UV at lamda max 260 nm. The standardization method will be published elsewhere.

  During analysis AKBA could not be detected in plasma samples. This might have been due to decomposition of AKBA in blood stream or in GI tract. It has been observed (Schweizer et al. 2000) that during extraction and workup of Boswellia serrata AKBA gets decomposed to 3-O acetyl-9,11-dehydro BA and 9,11-dehy dro BA (Both decomposed components have shown 5-LO inhibition). Hence all kinetic data was studied on KBA.

Statistical Analysis

After consultation with statistician, sample size of 12 was considered to be sufficient. All the concentrations were log transformed for calculation of various pharmacokinetic parameters except Area Under Curve (AUC). Data is shown as average with standard error of mean (SEM).

Assumption of normality and consistency of variance were explored in all analysis and were found to be valid.

Pharmacokinetic Analysis (Ritschel, 1980; Rowland and Tozer, 1995; Gibaldi and Perrier, 1975)

Non compartmental pharmacokinetic analysis of concentration time data was performed.

Actual blood collection times were used for all calculations. Maximum observed plasma concentration (C max) and the time to C max (t max) were determined by visual inspection of individual concentration versus time curves.

Area under the concentration versus time curve through C last, the last measurable concentration (AUC last) was calculated by linear trapezoidal method. Area under the concentration versus time curve, extrapolated to infinity (AUC0–∞) was calculated according to the following equation:

\[
AUC_{0-\infty} = AUC_{\text{last}} + C_{\text{last}} / Kel.
\]

The elimination rate constant (Kel) and elimination half life (t 1/2) were determined by log-linear regress on data from the terminal monoexponential phase of the concentration versus time profiles, while for calculating absorption rate constant (Ka) and absorption half life (t 1/2 a) method of residuals was used.

Assuming complete absorption, clearance (Cl) and Apparent Volume of Distribution (Vd) were calculated as Vd (L) = Dose / Kel . AUC0–\infty

\[
Cl (ml/min) = Kel . Vd / 60
\]

Safety Assessment

Participants were monitored for adverse reactions, if any, with special attention to epigastric pain, nausea, vomiting and diarrhea.
Results

Demography

All the enrolled 12 volunteers completed the study. Subjects were in the median age of 19 years with mean age being 21.92 ± 7.56 (range 18–45 years). They had the mean height of 174.17 ± 7.18 cm (range 165–190 cm) and the mean weight of 59 ± 9.19 kg (range 50–77 kg).

Pharmacokinetics

When plasma concentration of KBA versus time curve was plotted, it was seen that there was an initial steep rise in plasma concentration followed by a decline, which again rose to attain the peak, which was then followed by persistent fall (Fig. 1).

The plasma peak of KBA was seen at 4.5 ± 0.55 h ($t_{\text{max}}$) (mean ± SEM) after administration of drug and this occurred at the plasma concentration of $2.72 \times 10^{-3}$ ± 0.18 µmoles/ml ($C_{\text{max}}$).

The absorption half life ($t_{1/2 \ a}$) was found to be 2.35 ± 0.63 h. The plasma curve declined with elimination rate constant (Kel) averaging 0.171 ± 0.038 with corresponding elimination half life ($t_{1/2 \ b}$) of 5.97 ± 0.95 h. The AUC$_{0-\infty}$ averaged was $27.33 \times 10^{-3}$ ± 1.99 µmoles/ml. The plasma concentration of KBA was not detectable in four volunteers after 14 h of drug administration.

The apparent volume of distribution was found to be 142.87 ± 22.78 l. The plasma clearance averaged 296.10 ± 24.09 ml/min (Table 2).

Table 1. Plasma concentrations × 10$^{-3}$ (µmoles/ml) of 11-Keto β-Boswellic Acid in 12 volunteers.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>2.5</th>
<th>3</th>
<th>3.5</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vol. No</td>
<td>C1</td>
<td>C2</td>
<td>C3</td>
<td>C4</td>
<td>C5</td>
<td>C6</td>
<td>C7</td>
<td>C8</td>
<td>C9</td>
<td>C10</td>
<td>C11</td>
<td>C12</td>
<td>C13</td>
</tr>
<tr>
<td>1</td>
<td>0.00</td>
<td>0.00</td>
<td>1.68</td>
<td>2.57</td>
<td>3.91</td>
<td>3.53</td>
<td>3.67</td>
<td>2.25</td>
<td>1.56</td>
<td>1.06</td>
<td>0.86</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>2</td>
<td>1.89</td>
<td>2.08</td>
<td>1.17</td>
<td>0.79</td>
<td>0.64</td>
<td>0.85</td>
<td>1.09</td>
<td>1.62</td>
<td>1.41</td>
<td>1.19</td>
<td>1.28</td>
<td>0.96</td>
<td>0.78</td>
</tr>
<tr>
<td>3</td>
<td>0.89</td>
<td>1.17</td>
<td>1.67</td>
<td>1.64</td>
<td>1.57</td>
<td>1.35</td>
<td>2.15</td>
<td>2.25</td>
<td>1.84</td>
<td>1.24</td>
<td>1.05</td>
<td>0.89</td>
<td>0.81</td>
</tr>
<tr>
<td>4</td>
<td>1.79</td>
<td>0.95</td>
<td>0.71</td>
<td>1.17</td>
<td>0.97</td>
<td>1.42</td>
<td>1.56</td>
<td>1.73</td>
<td>2.18</td>
<td>1.19</td>
<td>1.05</td>
<td>0.90</td>
<td>0.92</td>
</tr>
<tr>
<td>5</td>
<td>0.83</td>
<td>0.67</td>
<td>2.65</td>
<td>3.25</td>
<td>3.56</td>
<td>3.42</td>
<td>3.77</td>
<td>3.27</td>
<td>1.75</td>
<td>2.40</td>
<td>1.02</td>
<td>1.33</td>
<td>0.00</td>
</tr>
<tr>
<td>6</td>
<td>1.70</td>
<td>1.50</td>
<td>1.11</td>
<td>1.50</td>
<td>1.81</td>
<td>2.12</td>
<td>2.84</td>
<td>1.99</td>
<td>2.73</td>
<td>1.06</td>
<td>1.11</td>
<td>0.79</td>
<td>0.67</td>
</tr>
<tr>
<td>7</td>
<td>0.34</td>
<td>0.40</td>
<td>0.33</td>
<td>0.72</td>
<td>0.81</td>
<td>1.09</td>
<td>1.34</td>
<td>2.03</td>
<td>2.39</td>
<td>2.00</td>
<td>1.95</td>
<td>1.40</td>
<td>1.51</td>
</tr>
<tr>
<td>8</td>
<td>0.76</td>
<td>1.64</td>
<td>0.24</td>
<td>2.44</td>
<td>2.42</td>
<td>2.16</td>
<td>2.41</td>
<td>3.10</td>
<td>1.79</td>
<td>1.11</td>
<td>1.70</td>
<td>1.40</td>
<td>1.26</td>
</tr>
<tr>
<td>9</td>
<td>1.04</td>
<td>1.09</td>
<td>1.00</td>
<td>1.01</td>
<td>1.41</td>
<td>1.23</td>
<td>1.26</td>
<td>1.30</td>
<td>1.20</td>
<td>2.56</td>
<td>1.22</td>
<td>0.97</td>
<td>0.95</td>
</tr>
<tr>
<td>10</td>
<td>1.82</td>
<td>1.18</td>
<td>1.29</td>
<td>2.26</td>
<td>1.52</td>
<td>0.96</td>
<td>0.93</td>
<td>0.88</td>
<td>0.99</td>
<td>1.09</td>
<td>1.45</td>
<td>0.59</td>
<td>0.00</td>
</tr>
<tr>
<td>11</td>
<td>0.70</td>
<td>0.60</td>
<td>1.32</td>
<td>1.18</td>
<td>1.23</td>
<td>2.16</td>
<td>1.22</td>
<td>1.00</td>
<td>0.86</td>
<td>0.86</td>
<td>0.77</td>
<td>0.69</td>
<td>0.00</td>
</tr>
<tr>
<td>12</td>
<td>1.84</td>
<td>1.60</td>
<td>1.03</td>
<td>1.47</td>
<td>3.07</td>
<td>2.62</td>
<td>2.71</td>
<td>2.65</td>
<td>3.18</td>
<td>1.70</td>
<td>1.40</td>
<td>1.30</td>
<td>1.21</td>
</tr>
<tr>
<td>Mean</td>
<td>1.13</td>
<td>1.07</td>
<td>1.18</td>
<td>1.67</td>
<td>1.91</td>
<td>1.91</td>
<td>2.08</td>
<td>2.01</td>
<td>1.82</td>
<td>1.46</td>
<td>1.24</td>
<td>0.94</td>
<td>0.68</td>
</tr>
<tr>
<td>SEM</td>
<td>0.33</td>
<td>0.31</td>
<td>0.34</td>
<td>0.48</td>
<td>0.55</td>
<td>0.55</td>
<td>0.60</td>
<td>0.58</td>
<td>0.53</td>
<td>0.42</td>
<td>0.36</td>
<td>0.27</td>
<td>0.20</td>
</tr>
</tbody>
</table>

SEM – Standard Error of Mean
C1, C2 – Concentrations at the given time

Table 2. Pharmacokinetic parameters after oral administration of 333 mg of BSE.

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameters</th>
<th>Mean</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{max}}$ (µmoles/ml)</td>
<td>$2.72 \times 10^{-3}$</td>
<td>0.18</td>
</tr>
<tr>
<td>$t_{\text{max}}$ (h)</td>
<td>4.5</td>
<td>0.55</td>
</tr>
<tr>
<td>Kel (per h)</td>
<td>0.17</td>
<td>0.04</td>
</tr>
<tr>
<td>$t_{1/2 \ a}$ (h)</td>
<td>5.97</td>
<td>0.94</td>
</tr>
<tr>
<td>AUC$_{0-\infty}$ (µmoles/ml)</td>
<td>$27.33 \times 10^{-3}$</td>
<td>1.99</td>
</tr>
<tr>
<td>Ka (per h)</td>
<td>0.62</td>
<td>0.17</td>
</tr>
<tr>
<td>$t_{1/2 \ b}$ (h)</td>
<td>2.35</td>
<td>0.63</td>
</tr>
<tr>
<td>Vd (l)</td>
<td>142.87</td>
<td>22.78</td>
</tr>
<tr>
<td>Cl (ml/min)</td>
<td>296.10</td>
<td>24.09</td>
</tr>
</tbody>
</table>

Fig. 1. Mean plasma concentration × 10$^{-3}$ of 11-Keto β-Boswellic Acid versus time.
**Tolerability**

BSE was well tolerated on oral administration, in single dose of 333 mg as capsule formulation, by all the volunteers. No adverse events were seen or reported during the trial or during the following week.

**Discussion**

This study was planned in healthy men volunteers with single oral dose of 333 mg BSE. Though, one research paper (Gupta et al. 1997) has mentioned about publishing the pharmacokinetic data of BSE, no data could be seen in spite of intensive Internet search. Therefore, we have reason to believe that ours is the first report being published on pharmacokinetics of BSE. Since there is no published study on pharmacokinetics of BSE, comparison is not possible.

It is known that acidic drugs are better absorbed from the stomach. BSE being acidic, may be rapidly absorbed from the stomach as is also supported by absorption half life. The first rise is suggestive of rapid absorption, followed by a small decline and further rise which then attains the peak.

BSE can cause gastro-intestinal (GI) irritation (Gupta et al. 1997). Hence we gave BSE after meals, since ethically it was not correct to deprive the volunteers of food and expose them to the risk, if any, of GI irritation. Same standard diet was given to all the volunteers, ruling out the subjective variation because of food, if any. Moreover, it is the extent of absorption, F, which is likely to be most affected by food rather than the rate.

Elimination half-life of nearly six hours is indicative that BSE needs to be given orally at the frequency of six hourly intervals. Kinetically KBA will attain the steady state plasma concentration after approximately 30 hours (Ritschel, 1980). Since various clinical studies (Kulkarni et al. 1991; Gupta et al. 1997, 1998) with BSE in the dose range of 300–350 mg at 8 hourly frequency have been reported effective, we believe that 333 mg of BSE, three times a day will give adequate therapeutic plasma concentration.

Though KBA was not detectable in four volunteers at 14 hours, the possibility of slower elimination after 14 hours cannot be ruled out.

In a single dose, BSE shows very high volume of distribution. It indicates that the drug either goes specifically to “deep” tissues in peripheral compartments or is stored or pooled somewhere in the peripheral compartment, such as fat or is bound to specific biological material (Ritschel, 1980).

Clearance of a drug from the body indicates the loss of drug. Total clearance comprises not only of renal excretion but all other pathways of excretion including loss of drug by metabolism. It helps in determining maintenance dose, depending upon required concentration at steady state, so that the therapeutic concentrations are maintained with drug input, which balances the drug loss from the body.

The kinetic data after oral administration of BSE needs to be compared with intravenous BSE along with determination of urinary concentration of its metabolites, with different dosage strength and single as well as multiple dosage administration to assess the pharmacokinetic parameters including oral bioavailability and renal clearance of BSE.

We intend to conduct an extended clinical trial of BSE in patients of osteoarthritis using pharmacokinetic and pharmacodynamic models.

**Conclusion**

The principal pharmacokinetic parameters derived from this study are essential to understand the time course of drug after its administration and will aid in determining the optimum dosage schedule for better therapeutic use. These parameters will provide a baseline for the further exploration of what the body does to the drug and the pharmacodynamic correlation. BSE is a safe drug and well tolerated on oral administration. No adverse effects were seen with this drug when administered as a single dose in 333 mg. Extended trial is being planned for clinical correlation using pharmacokinetic-pharmacodynamic model.

**Acknowledgements**

We gratefully acknowledge the support of Pharmanza (India) in providing drugs and materials needed for this study. Our thanks to all our colleagues Dr Sarang Dhatrak, Dr Ganesh Dakhale, Dr Chetna Shamkuwar, Dr Swati Sharma, Mrs K.J.Gharpure, Dr. Smrita Sontakke, Dr. Kavita Jaiswal, Dr Sonali Pimpalkhute, Dr Shweta Kharalkar, Dr Kumud Harle, Dr. Jyoti Parekh and Dr. Sucheta Ghule, who helped us in conducting this trial. We are thankful to Dr.Suresh Chari, Dr. Indrayani Apte, Dr. Leena Abhichandani, Dr. Madhur Gupta and Dr Reena Wagh for their biochemical support. We are grateful to Mr. Kulkarni for statistical review. We also thank Mr. R. B. Moon, Mr. C. K. Kanhere, Mr. U. C. Chouhan and Mr. Abhijeet Morkhe for their help.

**References**


Selected medicinal plants of India (1992) (A monograph of identity, safety, and clinical usage) compiled by Swami Prakashnanda Ayurved Research Centre (SPARC), Bombay, for Chemexil, Tata Press, India, 65–66

Address

V. Thawani, 14-A, Jeevan Jyoti, Clarke Town, Nagpur – 440 004, India

Tel.: +91-712-2522977 / 2557744;
Fax: Care +91-712-2559060

e-mail: thawani@nagpur.dot.net.in