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Pharmacokinetic Profile of Sabroxy® and It's Bioavailability Enhancement by Bioperine®

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ABSTRACT

Recent advances in bioavailability enhancement of herbal products by compounds that have bioenhancing properties have produced a shift in enhancing the therapeutic effect of the products. This study was undertaken to see the effect of Sabroxy® alone at its effective dose and with a bioenhancer, BioPerine® at half of the effective dose to determine the pharmacokinetic profile and compare it. The reduced concentration of the dose reduces the risks of physiological side-effects and also has an impact on reduction in pricing in therapies that benefits more people due to its low cost and better effectiveness. Sabroxy® is a standardized extract prepared from the dried bark of the Indian trumpet tree (Oroxylum indicum) that helps improve memory and support neuronal functions. The results of the first human trial on the cognitive-enhancing effects of Sabroxy® suggest that it is a promising herbal candidate for the improvement of cognitive function in older adults with cognitive complaints. BioPerine® is a natural ingredient, which significantly improves bioavailability and benefits of nutritive compounds . It is a patented standardized extract from the fruits of Piper nigrum (black pepper) containing not less than 95% piperine. BioPerine® has been awarded the GRAS (Generally Recognized As Safe) status. The objective of the present study was to determine the pharmacokinetic profiling of Sabroxy® at two doses ie, 60 mg/kg body weight in rats (equivalent to human dose of 500mg/day) and 30 mg/kg body weight in rats (equivalent to human dose of 250mg/day) and to evaluate the pharmacological potentiating effect of Sabroxy® Overall, this study demonstrated that addition of Bioperine® into Sabroxy® improves plasma concentration, PK parameters like AUC0-24h, and bioavailability of Oroxylin A when compared to stand alone Sabroxy® without Bioperine®
KEYWORDS: Sabroxy®, Bioavailability enhancement, Bioperine®, Oroxylum indicum

INTRODUCTION

Interaction between two or more therapeutic drugs or agents resulting in a pharmacologic response greater than individual responses to each drug is potentiation of a therapeutic effect . In recent research considerable importance is being given to interactions between different kinds of agonists and Bioenhancer mediating common pharmacologic effects and to those interactions that involve amplification of effects. The pharmacological potentiation of a bioenhancer agent may reduce the dose of the other and produce the same therapeutic effect as that of the other drug alone at higher dose. The reduced concentration of the dose will reduce the risks of physiological side-effects. This will also have an impact reduction in pricing of the product that benefits more people due to its low cost. Much research is being conducted throughout the world to develop drugs or agents that will reduce the concentrations for therapeutic applications.

Recent advances in bioavailability enhancement of herbal products by compounds that have bioenhancer activity have produced a shift in way of therapeutic effect. This study was undertaken to see the effect of Sabroxy® alone at its effective dose and with a bioenhancer, BioPerine® at half of the effective dose to determine the pharmacokinetic profile and compare it.

Currently treatment economics that are more affordable for sections of society are need of the hour and way to do that is achieve reduction of drug dosage and thus reduced side effects and lower costs, is to increase drug bioavailability.

Sabroxy® is a standardized extract prepared from the dried bark of the Indian trumpet tree (Oroxylum indicum), contains a minimum of 10% Oroxylin A, to help improve memory and to support neuronal functions. The plant has been utilized in various Ayurvedic medicinal preparations to support immune function, to support digestion

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and hunger, to reduce thirst, to ease nasal irritations etc [1]. The bark has history in Ayurveda and other folk remedies for uses ranging from quelling fevers to supporting respiratory health. Oroxylum indicum extract prevents chemotherapy-induced cognitive impairment in mice [2].Three important flavanones present in Sabroxy® are: Oroxylin A, Baicalein and Chrysin (Figure 1) (Sabinsa US Patent 10,555,982 Composition containing Oroxylin A and method of extraction thereof).

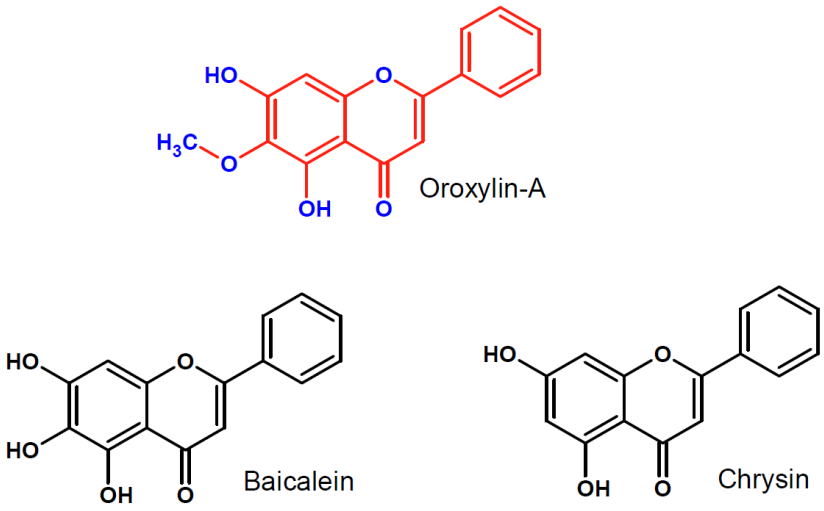


Figure 1: Three important flavanones present in Sabroxy® : Oroxylin A, Baicalein and Chrysin

The results of the first human trial on the cognitive-enhancing effects of Sabroxy® suggest that it is a promising herbal candidate for the improvement of cognitive function in older adults with self-reported cognitive complaints with a daily dose of 500mg [3].

BioPerine® a natural ingredient that significantly improves bioavailability, is a patented standardized extract from the fruits of Piper nigrum (black pepper) containing not less than 95% piperine. BioPerine® has been awarded the GRAS (Generally Recognized As Safe) status. BioPerine® emphasizes on the use of Piperine through oral, topical or parenteral administration for its role in improving gastrointestinal absorption and systemic utilization of nutrients and nutritional supplements [4]. It has been clinically tested with several nutrient groups, including fat-soluble vitamins (ß-carotene), water-soluble vitamins (vitamin B6, vitamin C), selenoamino acid [L(+)-Selenomethionine], coenzyme Q10 and shown to significantly enhance the bioavailability of supplemented nutrients through increased absorption. Herbal extracts such as curcumin has also been absorbed better when co-administered with BioPerine® [5]. The recommended dose of 5 - 10 mg per day contained in one serving of dietary supplements can help reap the benefits of Bioperine® with no significant side effects [6].

The objective of the present study was to determine the pharmacokinetic profiling of Sabroxy® at two doses ie, 60 mg/kg bwt (body weight) in rats (equivalent to human dose of 500mg/day) and 30 mg/kg bwt in rats (equivalent to human dose of 250mg/day) and to evaluate the pharmacological potentiating effect of Bioperine® at 0.6 mg/kg bwt (equivalent to human dose of 5mg/day) when given in combination with Sabroxy® at 30 mg/kg bwt in Sprague-Dawley rats.

MATERIALS AND METHODS

Sprague-Dawley female rats 10-12 weeks old weighing 180-200gms were used for the study. The animals were housed under standard laboratory conditions with adequate fresh air supply (Air changes 12-16 per hour), room temperature of 22 ± 3ºC, relative humidity at 30-70 %, with 12 hours light and 12 hours dark cycle. The temperature and relative humidity was recorded daily.

(a) STUDY DESIGN:

The animals were acclimatized to the laboratory conditions for 5 days and observations were made. One day before the start of study, the animals were allocated to 3 Groups viz., Group-I, Group-II and Group-III with 3 Sub-Groups each consisting of 3 animals in all the Sub-Groups. The animals were allotted by randomization and stratification to all the groups. The following Groups of animals with Sub-Groups for each of the test items were maintained (Table:1)

Table 1: Study design comprising grouping and dosing in animals

Test Item	Group	Dose (mg/kg Bwt)	Sub-Groups	No. of Animals
SABROXY®	GROUP-I	60	Group-1	3
			Group-2	3
			Group-3	3
SABROXY®	GROUP-II	30	Group-1	3
			Group-2	3
			Group-3	3
SABROXY® + **BIOPERINE®**	GROUP-III	30 + 0.6	Group-1	3
			Group-2	3
			Group-3	3

(b) ETHICS COMMITTEE APPROVAL

All experimental procedures used in present study were in accordance with the recommendation of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines for laboratory animals' and approved by Institutional Animal Ethics Committee (IAEC) protocol

(c) OBSERVATIONS

The following clinical observations were made during the study: Body Weights: Individual animal body weight was recorded at the beginning before administration of the test items.

Clinical signs and Pre-terminal Mortality: All the animals were observed for any clinical signs and pre-terminal deaths periodically at 15th min, 30th min, 1st h, 2nd h, 4th h 12 h and 24 h following dosing. The animals were constantly observed for any change in appearance and normal behaviour, change if any in behaviour were recorded. Observations including the changes in the skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, motor activity and behavior pattern were observed and recorded. Observations made were also directed at observation of tremors, convulsions, salivation, diarrhea, lethargy, anxiety and sleep.

Detailed Clinical Veterinary examination: The animals were subjected to detailed veterinary examination prior to test item administration and during the course of the study. The findings were recorded in standard formats. The animals were observed for the clinical signs on skin/fur, eyes, mucous membrane, occurrence of secretions & excretions, autonomic activities (lacrimation, piloerection, pupil size, papillary response, unusual respiratory response, response to handling, changes in gait, posture and behaviour.

(d) BLOOD SAMPLING FOR PHARMACOKINETIC PROFILING

In the present study 8 time points were selected to determine the pharmacokinetic profiling of the test items. The blood samples were collected humanely without causing pain and distress to the animals. Blood samples were collected from the animals from the retro orbital plexus prior to administration of test items ie., at 0 min [7]. Blood samples were drawn at 15 min, 30 min, 1 h, 2 h, 4 h, 12 h and 24 h after the Test items administration (Table 2) Blood samples were collected from the in di-potassium ethylene di-amine tetra acetic acid (K2-EDTA) anticoagulant. The blood samples were centrifuged at 3000 rpm for 10 minutes to obtain the plasma samples within one hour after the collection.

Table 2: Time points for the blood sample collection:

Test Item & Dose	Dose (mg/kg Bwt)	Group	Sub-Groups	No. of Animals	Blood Sampling Time Points = 8		
SABROXY®	60	GROUP-I	Group-1	3	0 min	1 hr	12 hr
			Group-2	3	15 min	2 hr	24 hr
			Group-3	3	30 min	4 hr	---
SABROXY®	30	GROUP-II	Group-1	3	0 min	1 hr	12 hr
			Group-2	3	15 min	2 hr	24 hr
			Group-3	3	30 min	4 hr	---
SABROXY® + **BIOPERINE®**	30 + 0.6	GROUP-III	Group-1	3	0 min	1 hr	12 hr
			Group-2	3	15 min	2 hr	24 hr
			Group-3	3	30 min	4 hr	---

Number of animals=3

(e) Plasma sample extraction

Plasma samples were prepared for LCMSMS analysis by using solid Phase Extraction (SPE) method**.** At the time of analysis, the samples were removed from the deep freezer and kept in the room temperature and allowed to thaw. NCSP - HLB - SPE cartridge and 30mg/mL solid phase extraction cartridge was conditioned with methanol, water sequentially. To this 500.0 µL aliquot of the plasma containing Oroxylin A were pipetted and loaded to the SPE cartridge. The cartridge was washed with 1.0mL of Milliq water twice. The drug was eluted from the cartridge using mobile phase (0.1 % Formic acid: Acetonitrile). The samples were injected to the LC-MSMS system for analysis [8].

(f) Calibration Curve preparation

A calibration (standard) curve is the relationship between instrument response and known concentrations of the analyte. A calibration curve should be generated for each analyte in the sample. A sufficient number of standards should be used to adequately define the relationship between concentration and response. A calibration curve should be prepared in the same biological matrix as the samples in the intended study by spiking the matrix with known concentrations of the analyte [9]. The number of standards used in constructing a calibration curve will be a function of the anticipated range of analytical values and the nature of the analyte/response relationship. Concentrations of standards should be chosen on the basis of the concentration range expected in a particular study. A calibration curve should consist of a blank sample (matrix sample processed without internal standard), and six to eight non-zero samples covering the expected range, including LLOQ [10]. The concentration ranges of calibration curve of Oroxylin A in Group I is 200 ng/ml to 5000 ng/ml and the r^2 is observed as 0.993. The concentration range of calibration curve of Oroxylin A in Group II & III is 200 ng/ml to 5000 ng/ml and the r^2 was observed as 0.999. Lower limit of Oroxylin A was 200 ng/ml.

(g) Pharmacokinetic parameter analysis

The pharmacokinetic parameters such as peak plasma concentration (C max), Time to peak Concentration (t max), and Area under the plasma concentration-time curve (AUC 0-t), were calculated based on plasma concentration over time by using pk1 and pk2 software.

(h) STATISTICAL ANALYSIS

The raw data was subjected to standard computer statistical processing wherever possible. The computer printout of the data (in the form of appendix) was verified with the original raw data file by the study group. The data was subjected to One-Way Anova standard statistical analytical procedures using Graphpad Prism software 8.4.2 (679).

The pharmacokinetic parameters such as peak plasma concentration (C max), Time to peak Concentration (t max), and Area under the plasma concentration-time curve (AUC 0-t), were calculated based on plasma concentration over time by using pk1 and pk2 software.

RESULTS

(a) Body Weights

The individual animal body weight was recorded at the beginning before administration of the test item. The summary of body weight measurements are presented in Table-3. There were no significant changes in the body weights in the animals after the test drug administration indicating that the Test item didn't have any adverse effects on body weight.

TABLE 3: Summary of Body weight of animals during initial and 24 hours after test item administration

BODY WEIGHT MEASUREMENTS					
Groups	**Test item**	**Test Dose (mg/kg bwt)**	**Sub Groups**	**Weekly Body weights (gm)**	
				Initial	**24 h after the Test items administration**
GROUP-I	SABROXY®	60	Group-1	187.5 ±5.53	**187.6 ±4.09**
			Group-2	187.6 ±4.62	**187.3 ±2.81**
			Group-3	187.4 ±4.51	**183.7 ±3.56**
GROUP-II	SABROXY®	30	Group-1	187.7 ±5.15	**187.2 ±6.36**
			Group-2	187.7 ±5.47	**185.9 ±3.57**
			Group-3	187.9 ±5.06	**186.0 ±4.69**
GROUP-III	SABROXY® + BIOPERINE®	30 + 0.6	Group-1	188.3 ±5.73	**190.3 ±4.78**
			Group-2	189.3 ±7.03	**190.2 ±7.57**
			Group-3	**190.4 ±7.77**	**190.3 ±8.10**

n=3;Values are presented in Mean ± SD

(b) Clinical signs and Pre-terminal Mortality

The clinical signs and pre-terminal deaths observation periodically at 10th min, 30th min, 1st h, 2nd h, 3rd h, 4th h and 6th h and thereafter for 24 h following dosing is depicted in Table-4. All the animals were found to be normal and healthy upon clinical signs during the study period. No toxicity or abnormal clinical signs were noticed in any of the animals during the observations in the study period.

TABLE 4: Summary of clinical signs and preterminal mortality observations in animals

CLINICAL SIGNS OBSERVATION RECORD											
Groups	**Test item**	**Test Dose (mg/kg bwt)**	**Sub Groups**	**Time Points**							
				0 min	**15 min**	**30 min**	**1 h**	**2 h**	**4 h**	**12 h**	**24 h**
GROUP-I	SABROXY®	60	Group-1-3	N	N	N	N	N	N	N	**N**
GROUP-II	SABROXY®	30	Group-1-3	N	N	N	N	N	N	N	**N**
GROUP-III	**SABROXY® + BIOPERINE®**	**30 + 0.6**	**Group-1-3**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**

n=3;N-Normal; D: Dead, h-hours

(c) Detailed Clinical Veterinary examination

The veterinary examination observations done prior to test item administration and thereafter during the study period are presented in Table-5.

All the animals were found to be normal in appearance and healthy upon detailed clinical veterinary examination during the study period. No abnormal behaviour or clinical signs were observed in any of the animals during the observations in the study period including the changes in the skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, motor activity and behaviour pattern that were normal.

TABLE 5: Summary of detailed clinical veterinary examination in animals

Sl No.	Groups		Group-I	Group-II	Group-III
	Test item		SABROXY®	SABROXY®	SABROXY® + BIOPERINE®
	Dose		60 mg/kg bwt	30 mg/kg bwt	30 + 0.6 mg/kg bwt
	Sex		Female	Female	Female
	No. of animals		3	3	3
1)	**Skin & Fur**		0	0	0
2)	**Eyes**		0	0	0
3)	**Mucous membrane**		0	0	0
4)	**Occurrence of secretions & excretions**	a. Salivation	0	0	0
		b. Urine Staining	0	0	0
		c. Fecal staining or diarrhoea	0	0	0
		d. Nasal discharge	0	0	0
5)	**Autonomic activity**	a. Lacrimation	0	0	0
		b. Piloerection	0	0	0
		c. Pupil size or Pupillary response	0	0	0
		d. Un-usual respiratory pattern	0	0	0
6)	**Response to handling**		0	0	0
7)	**Changes in gait**		0	0	0
8)	**Posture**		0	0	0
9)	**Clonic or Tonic movements**		0	0	0
10)	**Stereotypic behavior**	a. Repetitive circling	0	0	0
		b. Excessive grooming	0	0	0
11)	**Bizarre behavior**	a. Self mutilation	0	0	0
		b. Walking backwards	0	0	0

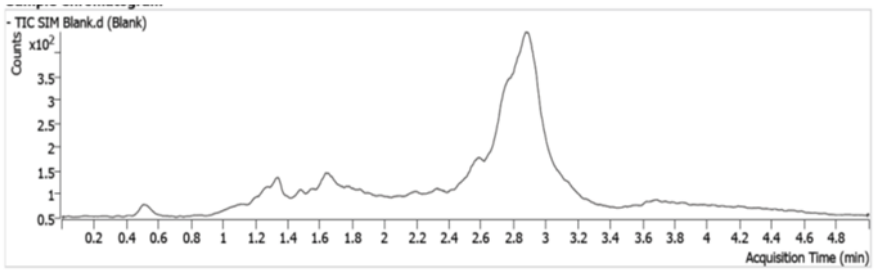
n=3 ; "0" – Absence of clinical sign

(d) Plasma Samples Pharmacokinetic LC-MSMS chromatograms:

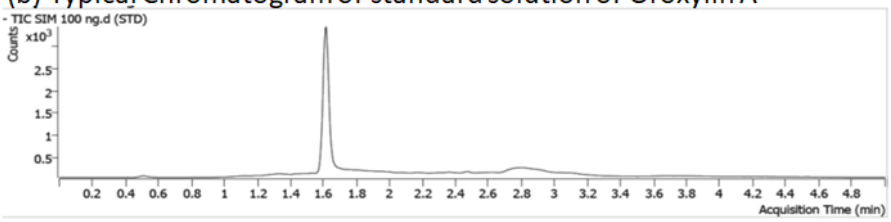
Figure 2(a) shows a typical LC-MSMS Chromatogram of Rat blank plasma solution. (b)Typical Chromatogram of standard solution of Oroxylin A and (c) Typical Chromatogram of Oroxylin A in sample solution

Figure 2:

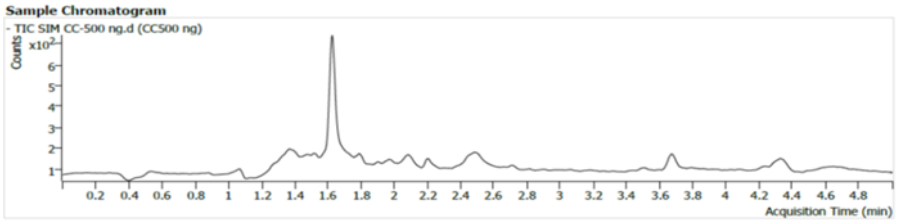
(a) Typical Chromatogram of Rat blank plasma solution



(b) Typical Chromatogram of standard solution of Oroxylin A

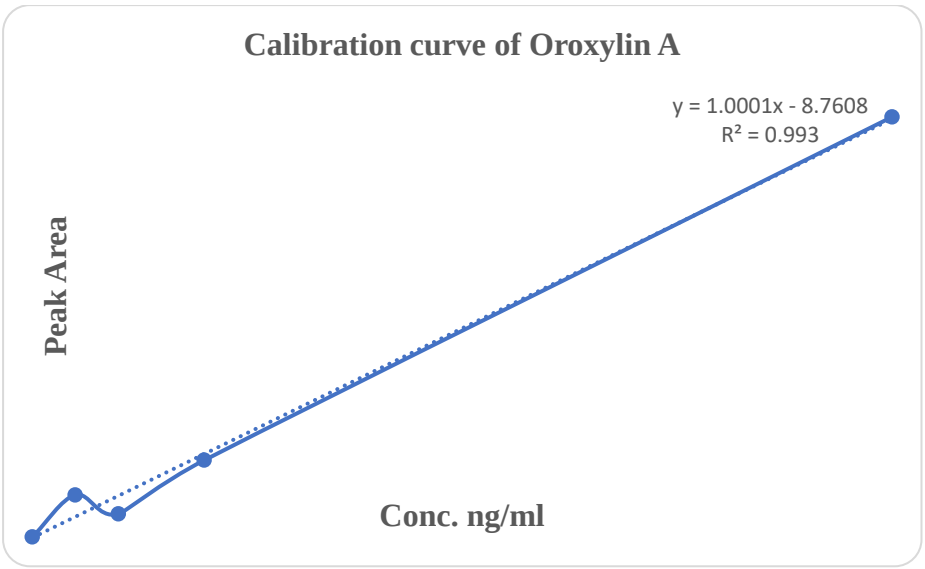


(c) Typical Chromatogram of Oroxylin A in sample solution



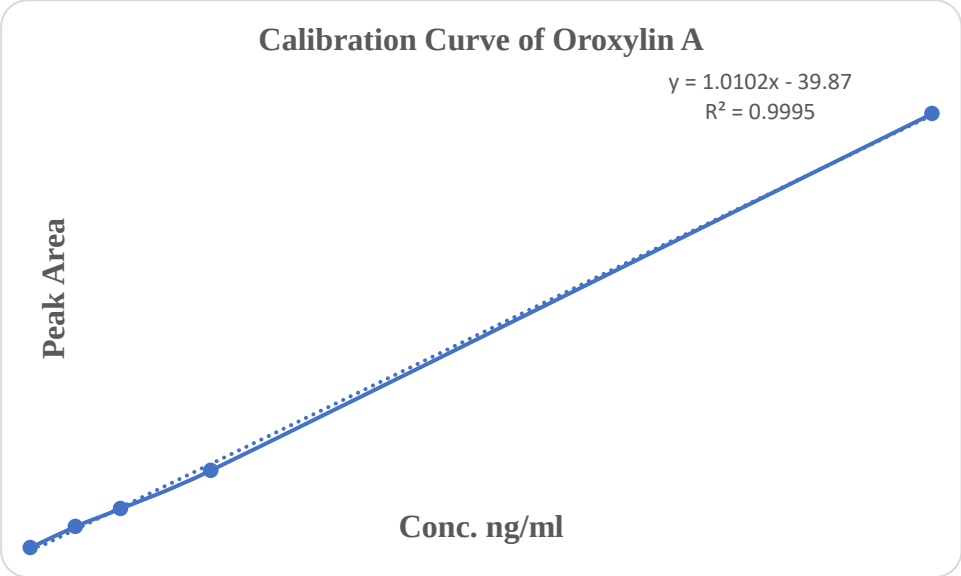
The following is the calibration curve of Oroxylin A in Blank Rat Plasma sample:

Figure 3(a): Calibration Curve of Oroxylin A in Blank Rat Plasma for Group-I



The following is the calibration curve of Oroxylin A in blank rat plasma for Group-II (Sabroxy® 30 mg/kg bwt) and Group-III (Sabroxy® 30 mg/kg bwt + Bioperine® 0.6 mg/kg bwt):

Figure 3 (b): Calibration Curve of Oroxylin A in Blank Rat Plasma for Group-II and Group-III Samples



(e) Determination of Pharmacokinetics parameters of Oroxylin A

Table 6: Plasma concentration of Oroxylin A at different time intervals (0 – 24 h)

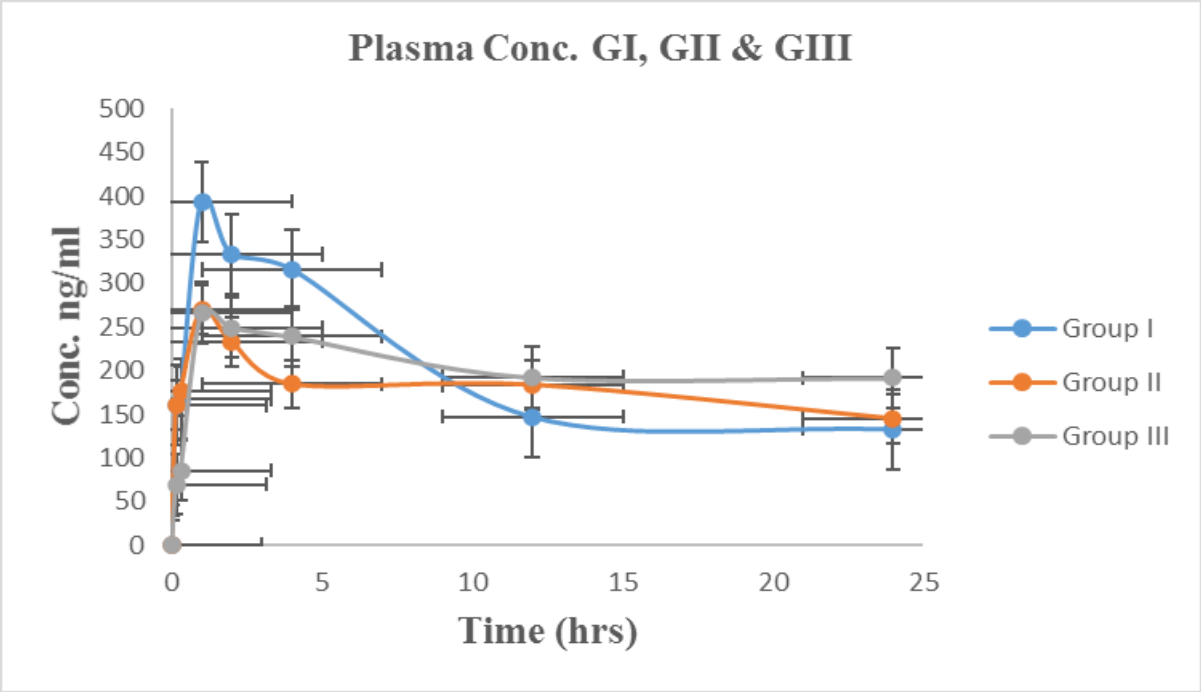
Time points (h)	GROUP-I (ng/ml)	GROUP-II (ng/ml)	GROUP-III (ng/ml)
0	0	0	0
0.15	160.3604 ± 16.3671	69.8030 ± 10.0545	160.9415 ± 18.6332
0.3	167.0447 ± 16.4634	85.4828 ± 44.8988	177.0334 ± 40.2921
1	393.9112 ± 496.1126	266.2061 ±41.5337	269.4916 ± 123.0195
2	333.0839 ± 356.7470	233.4973 ± 96.6897	249.6034 ± 122.6465
4	315.8771 ± 246.8124	184.6034 ± 35.3490	239.0684 ±35.9103
12	183.8650 ± 15.9758	147.0723 ± 107.8319	192.2857 ±43.1201
24	145.3991 ± 5.4161	133.1433 ± 111.8021	191.6725 ±68.6113

Table 7: Pharmacokinetic parameters of Oroxylin A

PK Parameters	Group I Sabroxy® 60 mg/kg bwt	Group II Sabroxy® 30 mg/kg bwt	Group III Sabroxy® 30 mg/kg bwt + Bioperine® 0.6 mg/kg bwt	Bioavailability Of Oroxylin A in Group-III compare to Group-II	Bioavailability Of Oroxylin A in Group-III compare to Group-I
$C_{max\ (ng/ml)}$	393.9112	266.2061	269.4916	**130 %**	**95 %**
$T_{max\ (hr)}$	1.0000	1.0000	1.0000		
$K_{el\ (hr)}$	0.0426	0.0273	0.0144		
$t_{1/2\ (h)}$	16.2678	25.3793	48.1989		
$AUC_{0-24\ (ng.hr/ml)}$	**5220**	**3816**	**4971**		
$AUC_{0-\infty\ (ng.hr/ml)}$	8632	8691	18299		

Cmax= Maximum plasma concentration of Oroxylin A; T max = Time to reach maximum plasma concentration of Oroxylin A;Kel = Elimination rate constant; t1/2 = Half life of Oroxylin A; AUC0-24 = Area under the curve 0-24 hrs of Oroxylin A; AUC0-∞ = Area under the curve zero to infinity of Oroxylin A
Data was compared statistically Group-I (Sabroxy® 60 mg/kg bwt) vs Group-III (Sabroxy® 30 mg/kg bwt + Bioperine® 0.6 mg/kg bwt) p values: Cmax 0.763, AUC0-24 0.950& AUC0-∞ 0.861 and Group-II (Sabroxy® 30 mg/kg bwt) vs Group-III (Sabroxy® 30 mg/kg bwt + Bioperine® 0.6 mg/kg bwt) p values: Cmax 0.812, AUC0-24 0.985&AUC0-∞ 0.806.
max

Figure 4: Group-I, Group-II & Group-III plasma concentration-time profile curve (0 – 24 hrs)



In case of Sabroxy® at 60 mg/kg bwt dose Cmax, Tmax, AUC0-24h and T1/2 of Oroxylin A were 393.9112ng/mL, 1h, 5220 ng.hr/mL and 16h respectively whereas in case of Sabroxy® at 30 mg/kg bwt dose Cmax, Tmax, AUC0-24h and T1/2 of Oroxylin A were 266.2061 ng/mL, 1h, 3816 ng.hr/mL and 16 h respectively as described in Table 7. Additionally in case of combination doses of Sabroxy® (30 mg/kg bwt) and Bioprine® (0.6 mg/kg bwt) the PK parameters like Cmax, Tmax, AUC0-24h and T1/2 of Oroxylin A were 269.4916 ng/mL, 1h, 4971 ng.hr/mL and 24 h respectively as described in Table 7.
The data were compared statistically, Group I (Sabroxy® 60 mg/kg bwt) vs Group III (Sabroxy® 30 mg/kg bwt) + Bioperine® 5 mg/kg bwt) and Group II (Sabroxy® 30 mg/kg bwt) vs Group III (Sabroxy® 30 mg/kg bwt + Bioperine® 0.6 mg/kg bwt). The p values for Cmax, AUC 0-24 and AUC 0-∞ in both the cases was found to be <1. The "p" values of Group-I (Sabroxy® 60 mg/kg bwt) vs Group-III (Sabroxy® 30 mg/kg bwt) + Bioperine® 5 mg/kg bwt) was Cmax - 0.763, AUC 0-24 h -0.950 & AUC0-∞ - 0.861 and the "p" values for Group-II (Sabroxy® 30 mg/kg bwt) vs Group-III (Sabroxy® 30 mg/kg bwt + Bioperine® 0.6 mg/kg bwt) was Cmax - 0.812, AUC0-24 h - 0.985 & AUC0-∞ - 0.806.
0-∞ was observed 0.861

Overall, this data demonstrated that the Cmax and AUC0-24h of Oroxylin A at 30 mg/kg dose of Sabroxy® was decreased by 1.5 and 1.4 fold compare to 60 mg/kg dose of Sabroxy® whereas in case of Group-III where 30 mg/kg Sabroxy® in combination of 0.6 mg/kg dose of Bioprine® was administered into rat through PO route the Cmax of Oroxylin A was similar to Group-II but was decreased ~1.5 fold compare to Group1. AUC0-24h of Oroxylin A in Group-III was almost similar to Group-I and 1.3-fold higher than Group-II. Hence, bioavailability of Oroxylin A in Group-III was 95% compared to Group-I and 130 % compared to Group-II.

DISCUSSION

The global focus of drug discovery is now on methods aimed at reducing drug dosage, and thus drug treatment cost for making treatments more affordable for wide sections of society. One way to achieve reduction in drug

dosage is to increase drug bioavailability. Bioavailability is the rate and extent to which a therapeutically active substance enters systemic circulation and becomes available at the required site of action. Methods of increasing bioavailability of a drug, correspondingly increase levels in the bloodstream, and thus the efficacy, which in turn reduces the drug dosage required to achieve a given therapeutic effect.

From the present study it can be concluded that the addition of 0.6 mg/kg Bwt dose of Bioperine® (human equivalent dose of 5mg /day) to 30 mg/kg bwt dose of Sabroxy® (human equivalent dose of 250mg /day) has enhanced overall plasma concentration, AUC0-24h of Oroxylin A compared to stand alone dose of Sabroxy® at 30 mg/kg bwt without Bioperine® . The plasma concentration, AUC0-24h of Oroxylin A in 30 mg/kg bwt dose of Sabroxy® in combination of 0.6mg/kg dose of Bioperine® was almost equivalent to that 60 mg/kg bwt dose of Sabroxy®(human equivalent dose of 500mg /day) .As a result bioavailability of Oroxylin A at 30 mg/kg bwt dose of Sabroxy in presence of 0.6 mg/kg bwt dose of Bioperine® was 130% compare to stand alone 30 mg/kg bwt dose of Sabroxy® without Bioperine® and 95% compare to 60 mg/kg bwt dose of Sabroxy®. Hence, this study has demonstrated that addition of Bioperine® into Sabroxy® has improved PK parameters like AUC0-24h, and bioavailability of Oroxylin A. Overall, this study demonstrated that addition of Bioperine® into Sabroxy® has improved plasma concentration, PK parameters like AUC0-24h, and bioavailability of Oroxylin A compared to stand alone Sabroxy® without Bioperine®.

Thus, addition of Bioperine® 5mg/kg enhances the bioavailability of Sabroxy® reducing the human dose of 500 mg to 250mg per day. Bioperine® is capable of enhancing bioavailability and bioefficacy of Sabroxy® with which it is combined reducing the effective dose of Sabroxy® to half.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

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