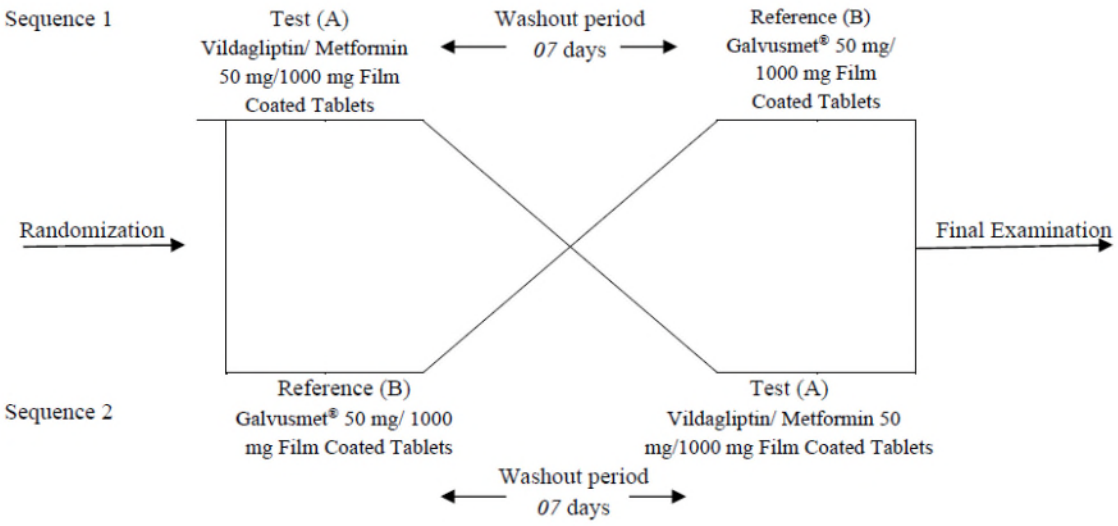
1. Participant Flow

Figure 1: Schematic Chart of the Study (Crossover Design)



10.1 Disposition of Subjects

Table 17 Disposition of subjects

Disposition	**Number of subjects**	
Total Number of subjects screened	**65**	
Withdrawals before enrolment	**25**	
Reasons		
Screen Failure: Abnormal lab result	17	
Blocked on JFDA database	02	
Screen Failure: Abnormal ECG	01	
Screen Failure: Abnormal BMI	02	
Personal Reason	03	
Total number of subjects enrolled	**(36) primary subjects+ 04 stand by subject**	
After enrollment	**Period I**	**Period II**
Total withdrawn before dosing	04 stand by subjects	00
Total number of subjects who received dose	36	36
Total withdrawn after dosing	00	00
Total Completed the Period	**36**	**36**

2. Baseline Characteristics

A total of 36 healthy, male, human Caucasian subjects from the Jordan population, 18 to 50 years old, eligible for participation as per the selection criteria of the protocol were enrolled in the study.

Thirty six (36) subjects have completed the study. Demographic data is summarized in the following table:

Table 19 Demographic Data

Parameter	Age (Years)	Height (m)	Weight (Kg)	BMI (Kg/m2)
N	36	36	36	36
Mean	29	1.74	76	24.9
SD	7.8	0.050	9.6	2.97
Min	18	1.62	58	20.3
Max	45	1.84	92	29.7

For details see below table:

14.1 Demographic Data

Table 27 Demographic data of the study subjects

Subject No.	Gender	Race	Age (years)	Height (m)	Weight (kg)	BMI (Kg/m^2)
01	Male	Caucasian	43	1.66	82	29.7
02	Male	Caucasian	25	1.75	75	24.4
03	Male	Caucasian	45	1.66	75	27.2
04	Male	Caucasian	33	1.71	66	22.5
05	Male	Caucasian	25	1.73	62	20.7
06	Male	Caucasian	32	1.74	69	22.7
07	Male	Caucasian	33	1.75	63	20.5
08	Male	Caucasian	18	1.76	90	29.0
09	Male	Caucasian	21	1.78	73	23.0
10	Male	Caucasian	19	1.71	71	24.2
11	Male	Caucasian	18	1.62	65	24.7
12	Male	Caucasian	31	1.74	85	28.0
13	Male	Caucasian	25	1.80	92	28.3
14	Male	Caucasian	22	1.82	74	22.3
15	Male	Caucasian	23	1.75	80	26.1
16	Male	Caucasian	27	1.83	90	26.8
17	Male	Caucasian	35	1.74	86	28.4
18	Male	Caucasian	39	1.75	83	27.1
19	Male	Caucasian	18	1.77	66	21.0
20	Male	Caucasian	28	1.80	70	21.6
21	Male	Caucasian	32	1.75	75	24.4
22	Male	Caucasian	25	1.78	77	24.3
23	Male	Caucasian	26	1.72	69	23.3
24	Male	Caucasian	33	1.75	90	29.3
25	Male	Caucasian	33	1.84	84	24.8
26	Male	Caucasian	45	1.74	84	27.7
27	Male	Caucasian	33	1.74	87	28.7
28	Male	Caucasian	40	1.74	69	22.7
29	Male	Caucasian	36	1.80	84	25.9
30	Male	Caucasian	19	1.68	58	20.5
31	Male	Caucasian	37	1.75	83	27.1
32	Male	Caucasian	20	1.77	68	21.7
33	Male	Caucasian	24	1.74	68	22.4
34	Male	Caucasian	24	1.80	80	24.6
35	Male	Caucasian	26	1.69	58	20.3
36	Male	Caucasian	33	1.65	81	29.7
N			36	36	36	36
Mean			29	1.74	76	24.9
SD			7.8	0.050	9.6	2.97
Min			18	1.62	58	20.3
Max			45	1.84	92	29.7

Outcome Measures:

Results for Vildagliptin:

Table 1 Summary of Vildagliptin Pharmacokinetic Parameters

Pharmacokinetic Parameter	Test Product (A) (mean ± SD) N=36	Reference Product (B) (mean ± SD) N=36
C_{max} (ng /ml)	76.54 ± 20.606	73.99 ± 21.526
AUC_{0-t} (hr*ng/ml)	358.56 ± 57.756	355.27 ± 69.553
Pharmacokinetic Parameter	**Test Product (A) (mean ± SD) N=34**	**Reference Product (B) (mean ± SD) N=35**
$AUC_{0-\infty}$ (hr*ng/ml)	378.17 ± 62.279	369.66 ± 68.677
T_{half} (hr)	2.22 ± 0.735	2.03 ± 0.567
$K_{elimination}$ (hr-1)	0.3396 ± 0.09300	0.3706 ± 0.11124
AUC_%Extrap_obs	4.47 ± 5.142	3.19 ± 2.993
Pharmacokinetic Parameter	**Test Product (A) (median ± SD), (Min-Max) N=36**	**Reference Product (B) (median± SD), (Min-Max) N=36**
T_{max} (hr)	2.50 ± 1.553, (0.75- 8.00)	2.50 ± 1.405, (0.50- 5.00)

Table 2 Statistical Comparisons of Vildagliptin Pharmacokinetic Parameters

Primary PK Parameter	Number of subjects	Intrasubject CV	Geometric LS Means		Ratio	90% Confidence Limits		Power
			Test (A)	Reference(B)		Lower	Upper	
C_{max}	36	19.91%	73.87	71.09	103.90	96.05	112.40	0.9981
AUC_{0-t}	36	10.12%	354.19	348.77	101.55	97.55	105.72	1.0000
$AUC_{0-\infty}$	33	8.32%	375.66	369.50	101.67	98.20	105.25	1.0000

Results for Metformin:

Table 3 Summary of Metformin Pharmacokinetic Parameters

Pharmacokinetic Parameter	Test Product (A) (mean ± SD) N=36	Reference Product (B) (mean ± SD) N=36
C_{max} (ng /ml)	1448.13± 397.346	1479.84±348.938
AUC_{0-t} (hr*ng/ml)	13340.49± 3305.003	13597.70±3486.835
Pharmacokinetic Parameter	**Test Product (A) (mean ± SD) N=35**	**Reference Product (B) (mean ± SD) N=36**
$AUC_{0-\infty}$ (hr*ng/ml)	13853.49± 3331.352	14153.50±3784.388
T_{half} (hr)	4.28± 0.519	4.52±1.030
$K_{elimination}$ (hr-1)	0.1640± 0.01948	0.1593±0.02752
AUC_%Extrap_obs	3.41± 3.254	3.63±3.095
Pharmacokinetic Parameter	**Test Product (A) (median ± SD), (Min-Max) N=36**	**Reference Product (B) (median± SD), (Min-Max) N=36**
T_{max} (hr)	4.00± 1.708, (1.00-8.00)	4.50±1.331, (0.75-6.00)

Table 4 Statistical Comparisons of Metformin Pharmacokinetic Parameters

Primary PK Parameter	Number of subjects	Intrasubject CV	Geometric LS Means		Ratio	90% Confidence Limits		Power
			Test (A)	Reference(B)		Lower	Upper	
C_{max}	36	13.12%	1398.75	1439.77	97.15	92.22	102.34	1.0000
AUC_{0-t}	36	11.36%	12936.80	13158.66	98.31	93.97	102.85	1.0000
$AUC_{0-\infty}$	35	10.99%	13470.20	13850.76	97.25	93.03	101.66	1.0000

Adverse Events reported in the study:

During the study, four (04) adverse events were reported in three (03) of the study subjects (8.33 %).

None of these AEs was serious and there were no AEs that resulted in any subject's death or occurrence of any other significant event.

All subjects with adverse events were completely recovered and no on-going adverse events.

Three (03) (75.00%) of the adverse events were reported after administration of test product A, and one (01) (25.00 %) of the adverse events was reported after administration of reference product B.

In terms of intensity: three (03) adverse events (75.00%) were considered as mild, and one (01) adverse event (25.00%) was considered as moderate.

- Three (03) (75.00%) of the adverse events were classified as probably related to the administered treatment:
  - ✓ Headache: (02 cases)

  Subjects no. 20: mild and probably related to test product.

  Subjects no. 21: mild and probably related to reference product.
  - ✓ Nausea: Subjects no. 25: moderate, probably related to test product.

- One (01) (25.00%) of the adverse events was classified as definitely related to the administered treatment:
  - ✓ Hypoglycaemia: Subjects no. 25: mild in intensity, definitely related to test product.

  Safety assessment conclusion:
  The adverse events reflect comparable safety profiles of Vildagliptin/ Metformin 50 mg/ 1000 mg Film Coated Tablets (Test Product/ Alpha Pharma, Kingdome of Saudi Arabia) and Galvusmet® 50 mg/ 1000 mg Film Coated Tablets (Reference Product/ Novartis Pharma, Switzerland.