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Research

Formulation and Evaluation of Alogliptin 12.5mg Immediate Release Tablets

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Abstract

The current research work predicts the applicability of QbD in manufacturing Alogliptin 12.5mg Tablets by using rate Disintegrants and diluent. From the results it was clearly apparent that as the disintegrate concentration increases. Grouping of disintegrate with other excipients do not interact with drug and vice versa, which informations to immediate delivery of drug. The improved formulation from factorial design can be used as a single dose per day. Bentonite was used successfully in preparing immediate release tablets containing alogliptin. However, this was possible only with aid of hydroxypropyl methylcellulose (HPMC). Furthermore, this study revealed the effect of benzoate on the crystalline bentonite structure and, as a result, the building gel structure of bentonite in water was hindered. Different used binders did not help to maintain the gel structure except by using HPMC. Dry and wet granulation procedure was the chosen technology for the preparation of tablet. Based on the preliminary studies, different formulation trials (F1-F7) were carried out with different concentrations of disintegrants, diluents. From the various formulations it was decided that the formulation batch of F7 was finalized as the optimized formula. Formulation F7 showed satisfactory results with various physicochemical evaluation parameters like Disintegration time, Dissolution profile, Assay when matched with that of the marketed product. The stability studies at all condition, indicates that the formulated capsules were found to be stable. Hence, it is finally concluded that, tablet are pharmaceutically comparable, low cost, quality improved and stable formulation.

Keywords: Alogliptin, Formulation, Evaluation, Diabetes mellitus

INTRODUCTION

Diabetes Mellitus (DM) is a widespread chronic metabolic disorder characterized by high blood glucose levels due to the body's inability to produce or effectively use insulin. This condition is primarily categorized into Type 1 diabetes, which results from autoimmune destruction of pancreatic beta cells that produce insulin, and Type 2 diabetes, marked by insulin resistance and insufficient insulin production. Type 2 diabetes accounts for approximately

90% of diabetes cases globally and has been increasing in prevalence, particularly in developing nations. This rise underscores the urgent need for effective treatments to help patients achieve and maintain glycemic control.

The primary focus of Type 2 diabetes management is to optimize blood glucose levels, minimize the risk of complications, and enhance patients' quality of life. Common therapeutic approaches include lifestyle modifications, insulin, and various oral hypoglycemic agents (OHAs), like metformin, sulfonylureas, and thiazolidinediones. Advances in diabetes treatment have led to newer drug classes such as Dipeptidyl Peptidase-4 (DPP-4) inhibitors, which are recognized for their effective glycemic control and relatively low risk of side effects.

Alogliptin is a potent DPP-4 inhibitor approved for Type 2 diabetes management. By selectively inhibiting the DPP-4 enzyme, alogliptin increases the levels of incretin hormones like GLP-1 (glucagon-like peptide-1) and GIP (gastric inhibitory polypeptide), which play critical roles in regulating blood glucose. These hormones stimulate insulin release after meals and reduce glucagon secretion, helping to control postprandial blood glucose levels. Alogliptin's high selectivity and effectiveness as a DPP-4 inhibitor make it an appealing option for patients who need blood glucose control with minimal side effects, such as hypoglycemia or weight gain.

Immediate-release tablet formulations of alogliptin are designed for rapid action, making them useful for managing postprandial glucose spikes. Immediate-release formulations dissolve quickly in the gastrointestinal tract, allowing for faster absorption and onset of therapeutic effects. For alogliptin, this characteristic is particularly advantageous since it enhances blood glucose control after meals. Additionally, these formulations support patient compliance, a vital component in chronic disease management, by offering a quick and convenient dosing option.

The goal of this project is to develop and evaluate a 12.5 mg immediate-release tablet formulation of alogliptin with optimal pharmacokinetic and pharmacodynamic properties. Developing this formulation involves overcoming several technical challenges, such as achieving rapid disintegration and dissolution, ensuring content uniformity, and maintaining the tablet's stability over time. These factors require careful selection and optimization of excipients to achieve the desired properties without compromising the stability or efficacy of the drug.

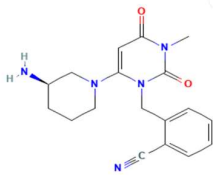
The aim of the study is the formulation and evaluation of alogliptin 12.5 mg immediate release tablets. The primary objective of this study is to develop and evaluate alogliptin 12.5 mg immediate-release tablets, with a focus on creating a stable, optimized formulation that ensures rapid disintegration and efficient drug release, leading to optimal bioavailability for effective management of Type 2 diabetes mellitus. The study aims to select and optimize excipients, such as binders, fillers, disintegrants, and lubricants, to achieve the desired tablet properties, including strength, dissolution rate, and stability. Additionally, the objective is to conduct comprehensive in vitro evaluations, including dissolution, disintegration, hardness, and stability testing, to assess the formulation's performance and consistency in providing the required therapeutic dose.

The ultimate goal is to develop a high-quality immediate-release tablet that ensures rapid and consistent therapeutic effects, supports effective postprandial glycemic control, and enhances patient compliance by offering an easy-to-use, stable, and reliable treatment option for Type 2 diabetes management.

MATERIALS AND METHODOLOGY

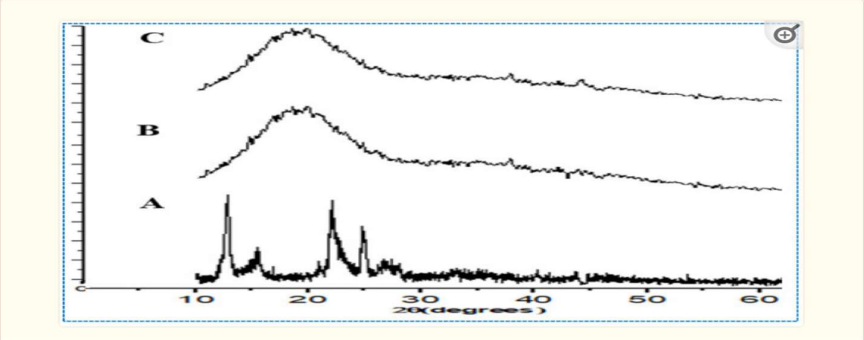
Alogliptin Benzoate, Cellulose Microcrystalline USP NF, Mannitol, Croscarmellose sodiumHydroxy Propyl cellulose Magnesium Stearate Magnesium Stearate Vibratory Sifter Rapid Mixture granulator 1000 l, Fluid Bed Dryer, Multimill, Octagonal blender, Tablet compression Machine, Tablet deduster, Metal detector Analytical balance, Vernier caliper ,Bulk density apparatus, Moisture analyzer.

Drug profile



Alogliptin is an oral medication used for managing Type 2 diabetes, acting as a Dipeptidyl Peptidase-4 (DPP-4) inhibitor to regulate blood glucose levels. It works by enhancing insulin secretion and reducing glucagon release after meals. As part of its pharmaceutical profile, its solubility, crystalline structure, and chemical composition are key to formulating effective dosage forms.

Drug Class: Dipeptidyl Peptidase-4 (DPP-4) Inhibitor,
Molecular Formula: C18H21N5O2
Molecular Weight: 329.4 g/mol,
Melting Point: Approximately 178°C,
Optical Rotation: +25° (C = 1, methanol)



Fourier Transform Infrared (FTIR) Spectroscopy Analysis

FTIR spectroscopy is employed to analyze the functional groups present in alogliptin by measuring its molecular vibrations. This technique provides a spectral fingerprint of the molecule, which is essential for assessing its purity and identifying possible impurities or interactions with excipients.

FTIR Results: The FTIR spectrum of alogliptin displays key absorption bands corresponding to functional groups such as amine (-NH2), thiazole (C-S), and pyrazole (C=N) groups. These characteristic peaks confirm the chemical structure of alogliptin and can also be used to detect any potential impurities or confirm the compatibility of alogliptin with other components in its formulation.

In conclusion, both XRD and FTIR provide vital information regarding the physical form and chemical structure of alogliptin, which is essential for optimizing its formulation, ensuring stability, and improving its bioavailability. These analyses contribute to the quality control and consistency of alogliptin as a pharmaceutical compound.

Sr.No	Test	Methods
Granulation :		
1.	Loss of Drying	Performed in moisture analyzer balance
2.	Bulk density	Measurement of Bulk density was done by pouring powder into a measuring cylinder through sieve # 20 and the initial weight was noted. The initial volume was termed as bulk volume.11
3.	Tapped density	Tapped density is defined as the ratio between aggregate weights of granules to the tapped volume of powder. Measurement of the volume was done by tapping the granules 750 times. If the variance in volume exceeds 2%, further tapping should be done for 1250 times. It was conveyed in g/ml
4.	Angle of Repose	Angle of repose was done by using powder flow tester. Angle of repose can be calculated by measuring the height and radius of the pile of granules
5.	Compressibility index	It demonstrates the flow properties of the granules. It is conveyed in the form of % and can be calculated using bulk density and tapped density.
6.	Hausner Ratio	Hausner ratio is an indirect way of accessing the ease of granules flow. It can be calculated by using bulk density and tapped density
Compression		
7.	Weight Variation	Randomly 20 tablets were selected and weighed using a single balance. Standard deviations were calculated and checked with the standard pharmacopeial limits.
8.	Thickness	Tablets were selected randomly from all batches and measurement of thickness was done by using Vernier Calliper.1
9.	Hardness	The strength of tablet is expressed in the form of tensile strength (Kg/cm2). The amount of force required to break the tablets was measured by using a hardness tester
10.	Friability	Randomly 20 tablets were selected and weighed from all the batches. The weighed tablets then placed in friabilator and then ran for 100 revolutions. After completion of 100 revolutions tablets were de-dusted, re-weighed and %friability was calculated.

Selection of the Raw material during formulation of the product

All the excipients used are well known and widely used as pharmaceutical excipients in oral soild formulations and comply with the relevant pharmacopoeia monographs. Compatibility studies were conducted to investigate and predict physicochemical interaction between drug substance and excipients and consequently excipients.

Selection of excipient in product formulation

Justification for excipient selection

However, during development studies, an excipient compatibility study was conducted for all excipients. Binary mixtures of API and excipients were subjected to 25°C / 60% RH (open and closed condition), 40°C / 75% RH (open and closed condition), 60°C and UV light. The results of excipient compatibility studies show no color change, no evidence of physical change and no significant change in related compound levels throughout the study for all proposed. Manufacturing Process.

Steps involved in manufacturing process

Following steps are involves in the manufacturing process involving usage appropriate equipment

Environmental condition: Like temperature, relative humidity and differential pressures needs to monitored during the entire manufacturing activity before giving line clearance and during activity. The observations were found within the limits mentioned in batch record. (i. NMT Temperature NMT 25 ºC , RH NMT65 % and Pressure difference .0-4.0 mm of wc)

Dispensing: All raw material are used un the batches are dispensed as per the approved standard procedure and defined batch record and each stage is recorded in the batch record .

Sifting: Sifting of raw material is done as per the batch record using the mesh #20 during activity and same is recorded in the batch record. Integrity of the batch is cheeked before and after sifting.

Dry Mixing: Load the material in the RMG and mixed for5 minutes with impeller at slow speed and chopper off and record the amperage reading

Binder preparation: Hydroxy propyl cellulose was dissolved in purified water

Wet granulation: Is done addition of the purified water into the RMG to form the granules and get the desired content of mass and drug.

- Take the purified water and add over of period of 5 minutes while mixing with impeller at slow speed and chopper off and record the amperage reading and record in batch record.
- End points where the granulation is the formation of wet granules
- Scrape the impeller and inner walls of the bowl using scraper and continue the mixing for 2 minutes with impeller and chopper at slow speed and record the amperage reading if impeller and chopper.
- Discharge the wet mass in the fluid bed through the co mill with 2.0mm screen

Drying: The wet mass air dried for 5 minutes to ensure fluidization in FBD. Dried at the inlet temperature of 65± 5 ºC till the loss of drying reached in the range of NMT 2.0% at 105ºC in the moisture analyzer.

Sifting and Milling: The dried granules are sifting through mesh #20 and the retension are milled through multimill with 1.5 mm screen at slow/ speed/ knives forward direction and sifted through mesh # 20.

Lubrication: Extra granular material – Croscarmellose sodium sifted through mesh # 60 and loaded into the octagonal blender and rotated at 5 minute at 10 RPM and after blending sample is tested from 10 different location for the blend uniformity

Compression: Compression is done at the compaction forces to active the desired results

Table 1: Different quantity of ingredient were change for the formulation to optimized the formula

Ingredient	**Quantity in batch per kg (mg/Tablets)**						
	Trail 1	**Trail 2**	**Trail 3**	**Trail 4**	**Trail 5**	**Trail 6**	**Trail 7**
Dry Mixing							
Alogliptin USP	34	34	34	34	34	34	34
Cellulose Microcrystalline USP NF	38.5	36.53	36.83	36.83	37.13	36.83	36.83
Mannitol	81.78	83.75	83.75	84.75	84.75	83.75	83.75
Croscarmellose sodium	5.1	5.1	4.8	3.8	3.5	4.8	4.8
	Granulation				**Total**	159.380	159.380
Hydroxy Propyl cellulose	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Purified water	70.00	70.00	70.00	70.00	70.00	70.00	70.00
	Extra Granular Ingredients						
Croscarmellose sodium	3.3	3.5	3.2	3.5	3.3	3.6	3.6
Magnesium Stearate	2.8	2.6	2.9	2.6	2.8	2.5	2.5
						170.00	
Coating							

Table 1: Different quantity of ingredient were change for the formulation to optimized the formula

Ingredient	Quantity in batch per kg (mg/Tablets)						
	Trail 1	**Trail 2**	**Trail 3**	**Trail 4**	**Trail 5**	**Trail 6**	**Trail 7**
Opadry white	2.125	2.125	2.125	2.125	2.125	2.125	
Purified water	19.125	19.125	19.125	19.125	19.125	19.125	
Total tablet weight						**87.125**	
Flow Properties	Very Poor	Poor	Passable	Fair	Good	Excellent	Excellent

Granulation Critical Process Parameter

Granulation control	**Trail 1**	**Trail 2**	**Trail 3**	**Trail 4**	**Trail 5**	**Trail 6**	**Trail 7**
Total Drying time	05 min	05 min	05 min	05 min	05 min	05 min	05 min
Inlet Granulation Stage temperature of FBD	69-72	68-69	99-65	62-65	69-72	65-75	65-72
Out let temperature of FBD	20-32	29-35	29-75	30-80	40-75	37-75	35-72
Impeller Speed (RPM 50)	50	50	50	50	50	50	50
Amperage Impeller	10	10	10	10	10	10	10
Chopper off	Off	Off	Off	Off	Off	Off	Off
Amperage Impeller	12	12	12	12	12	12	12
Chopper ON slow RPM 1500	04	04	04	04	04	04	04
Blender RPM	5	5	5	5	5	5	5
Blending time	10	10	10	10	10	10	10
Loss of Drying	2.0	1.2	1.1	1.2	1.2	1.1	1.1
Bulk density(g/ml)	0.451	0.432	0.425	0.424	0.489	0.453	0.458
Tapped density (g/ml)	0.242	0.317	0.492	0.431	0.421	0.654	0.643
Angle of Repose	8	47	43	38	33	28	28
Carrs Index	34	27	23	18	14	<10	<10
Hausner Ratio	1.36	1.26	1.25	1.22	1.2	0.8	0.7
Flow Properties	VeryPoor	Poor	Passable	Fair	Good	Excellent	Excellent
Compressibility index (%)	31.801	37.995	29.595	67.695	37.995	38.804	38.804
Water Content by KF	2.25	2.85	2.60	2.50	2.31	2.65	2.65

From the above table all in process control and parameter is observed well within criteria for Trail batches Trail 6 and Trail 7.

Weight of 10 tablets in grams	0.850 gm (0.816 -0.884)	0.856	0.864	0.856	0.879	0.862	0.878	0.872
Weight variation of individual tablet	85.00 (78.63- 91.73)	Min 86.38 Max 90.78	Min 86.69 Max 90.78	Min 86.82 Max 91.50	Min 86.59 Max 90.55	Min 86.59 Max 90.18	Min 86.59 Max 90.14	Min 86.59 Max 90.04
FriabilityAbout 650 gm tablets	NMT 1.0%	1.26	1.30	1.10	1.20	1.02	0.07	0.06
Thickness	6.50mm -8.00	Min 6.62 Max 7.63	Min 6.82 Max7.65	Min 5.78 Max 7.52	Min 6 .22 Max 7.02	Min 6.28 Max 7.25	Min 6.62 Max 6.64	Min 6.64 Max 6.67
Coating								
Pan Speed	2.0-5.0 RPM	4	4	4	4	4	4	4
Spray rate	15-50 g/gun/min	18-30	18-30	18-30	18-30	18-30	18-30	18-30
Air pressure	1-6 kg/cm2	2-4	2-4	2-4	2-4	2-4	2-4	2-4
Tablet weight gain	2.50 (2.00-3.00%)	2.38	2.25	2.36	2.35	2.47	2.56	2.55

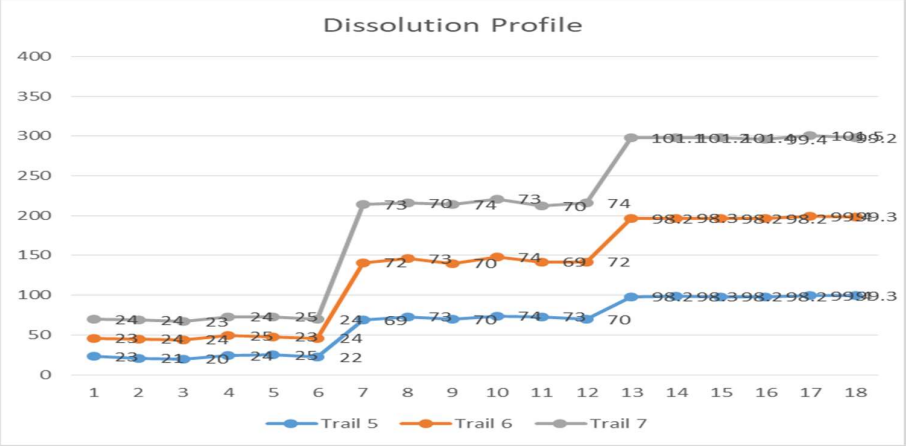
Issolution Profile of Un coated Tablets

Dissolution	**Trail 5**	**Trail 6**	**Trail 7**
1	99.44	99.67	99.67

2	99.56	99.59	99.59
3	100.05	99.55	99.55
4	99.42	99.38	99.38
5	99.64	99.48	99.48
6	99.83	99.69	99.69
Mean	99.66	99.65	99.56
SD	0.24	0.12	0.12
%RSD	0.24	0.12	0.12
HPLC	QC-HPLC002	QC-HPLC002	QC-HPLC002
Column	QC-COL-008	QC-8COL-00	QC-COL-008

Dissolution :in pH Phosphate buffer and 2% SLS at 75 RPM USP 1 for coated tablet

	Time	Specification	Trail 5	Trail 6	Trail 7
1	10minute	NMT 30%	23	23	24
2			21	24	24
3			20	24	23
4			24	25	24
5			25	23	25
6			22	24	24
1	20 min	Between 60-80%	69	72	73
2			73	73	70
3			70	70	74
4			74	74	73
5			73	69	70
6			70	72	74
1	30 minute	NLT 80 %	98.2	98.2	101.1
2			98.3	98.3	101.2
3			98.2	98.2	101.4
4			98.2	98.2	99.4
5			99.4	99.4	101.5
6			99.3	99.3	99.2



SUMMARY

This study centers on the formulation and evaluation of Alogliptin 12.5 mg Immediate-Release Tablets to improve therapeutic effectiveness in Type 2 diabetes management. Alogliptin, a DPP-4 inhibitor, requires immediate-release functionality to ensure prompt absorption and timely blood glucose control.

The formulation process involves the careful selection of excipients, including hydroxypropyl cellulose (HPC) for binding and film formation, microcrystalline cellulose and mannitol for structural support, crosscarmellose sodium for rapid disintegration, and magnesium stearate as a lubricant. Each excipient contributes to the tablet's stability, structural integrity, and immediate-release profile.

Extensive evaluation tests were conducted to determine tablet hardness, disintegration time, dissolution rate, and stability across various conditions. The results show that the tablets meet quality standards for immediate release, offering efficient and quick drug release, durability, and consistent performance.

In summary, this study successfully develops a stable, effective immediate-release Alogliptin tablet that supports rapid absorption, improved therapeutic outcomes, and reliable blood sugar control for patients with diabetes.

CONCLUSION

In conclusion, this project successfully developed and assessed Alogliptin 12.5 mg Immediate-Release Tablets to fulfill therapeutic requirements for Type 2 diabetes patients. The chosen excipient blend, particularly hydroxypropyl cellulose (HPC) as a binder and film-forming agent, along with microcrystalline cellulose, mannitol, Croscarmellose sodium, and magnesium stearate, contributed to the tablet's stability, efficient disintegration, and immediate-release properties. The evaluation confirmed that the tablets met the required hardness, rapid disintegration, and optimal dissolution parameters, aligning with quality standards for immediate-release formulations. This facilitates quick drug release and absorption, essential for effective blood sugar management in diabetes. Overall, the study demonstrates that this immediate-release Alogliptin tablet formulation is both reliable and effective, providing a viable solution for improving treatment adherence and therapeutic outcomes in diabetes management. This formulation marks an important advancement in enhancing the quality and efficacy of diabetes treatments.

REFERENCES

1. Ozougwu J., Obimba K., Belonwu C., Unakalamba C. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. J. Physiol. Pathophysiol. 2013;4:46–57. doi: 10.5897/JPAP2013.0001. [CrossRef] [Google Scholar]
2. Covington P., Christopher R., Davenport M., Fleck P., Mekki Q.A., Wann E.R., Karim A. Pharmacokinetic, pharmacodynamic, and tolerability profiles of the dipeptidyl peptidase-4 inhibitor alogliptin: A randomized, double-blind, placebo-controlled, multiple-dose study in adult patients with type 2 diabetes. Clin. Ther. 2008;30:499–512. doi: 10.1016/j.clinthera.2008.03.004. [PubMed] [CrossRef] [Google Scholar]
3. Said S., Nwosu A., Mukherjee D., Hernandez G. Alogliptin—A review of a new dipeptidyl peptidase-4 (DPP-4) inhibitor for the treatment of type 2 diabetes mellitus. Cardiovasc. Hematol. Disord. -Drug Targets. 2014;14:64–70. doi: 10.2174/1871529X14666140701095849. [PubMed] [CrossRef] [Google Scholar]
4. Uppal S., Italiya K.S., Chitkara D., Mittal A. Nanoparticulate-based drug delivery systems for small molecule anti-diabetic drugs: An emerging paradigm for effective therapy. Acta Biomater. 2018;81:20–42. doi: 10.1016/j.actbio.2018.09.049. [PubMed] [CrossRef] [Google Scholar]
5. Bhakay A., Rahman M., Dave R.N., Bilgili E. Bioavailability Enhancement of Poorly Water-Soluble Drugs via Nanocomposites: Formulation-Processing Aspects and Challenges. Pharmaceutics. 2018;10:86. doi: 10.3390/pharmaceutics10030086. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Kwok P.C., Chan H.K. Nanotechnology versus other techniques in improving drug dissolution. Curr. Pharm. Des. 2014;20:474–482. doi: 10.2174/13816128113199990400. [PubMed] [CrossRef] [Google Scholar]
7. Raghavan S.L., Schuessel K., Davis A., Hadgraft J. Formation and stabilisation of triclosan colloidal suspensions using supersaturated systems. Int. J. Pharm. 2003;261:153–158. doi: 10.1016/S0378-5173(03)00299-0. [PubMed] [CrossRef] [Google Scholar]
8. Hecq J., Amighi K., Goole J. Development and evaluation of insulin-loaded cationic solid lipid nanoparticles for oral delivery. J. Drug Deliv. Sci. Technol. 2016;36:192–200. doi: 10.1016/j.jddst.2016.10.012. [CrossRef] [Google Scholar]
9. Yin J., Hou Y., Yin Y., Song X. Selenium-coated nanostructured lipid carriers used for oral delivery of berberine to accomplish a synergic hypoglycemic effect. Int. J. Nanomed. 2017;12:8671–8680. doi: 10.2147/IJN.S144615. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Wang Q., Wei C., Weng W., Bao R., Adu-Frimpong M., Toreniyazov E., Ji H., Xu X.-M., Yu J. Enhancement of oral bioavailability and hypoglycemic activity of liquiritin-loaded precursor liposome. Int. J. Pharm. 2021;592:120036. doi: 10.1016/j.ijpharm.2020.120036. [PubMed] [CrossRef] [Google Scholar]