1st International Electronic Conference on Medicinal Chemistry

2-27 November 2015

chaired by Dr. Jean Jacques Vanden Eynde

sponsored by pharmaceuticals

Floating Drug Delivery Systems with Xanthan Gum, Eudragit-RS PO or Lubritose SD: Nizatidine and Piracetam as Model Drugs

Azhidhack Hadjipour, Rena-Jean Palmer, Mohamed Zarara, Amal Ali Elkordy*

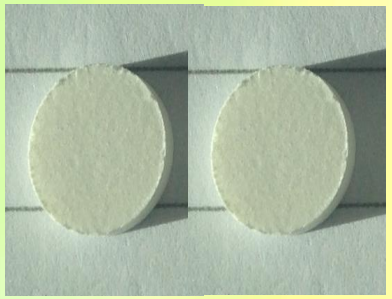
*Dr. Amal Ali Elkordy, Reader in Pharmaceutics

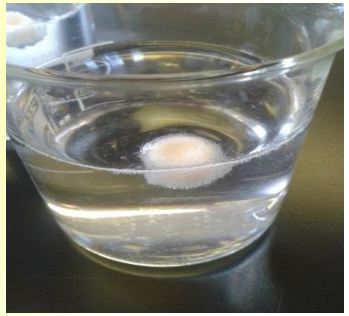
Sunderland Pharmacy School,

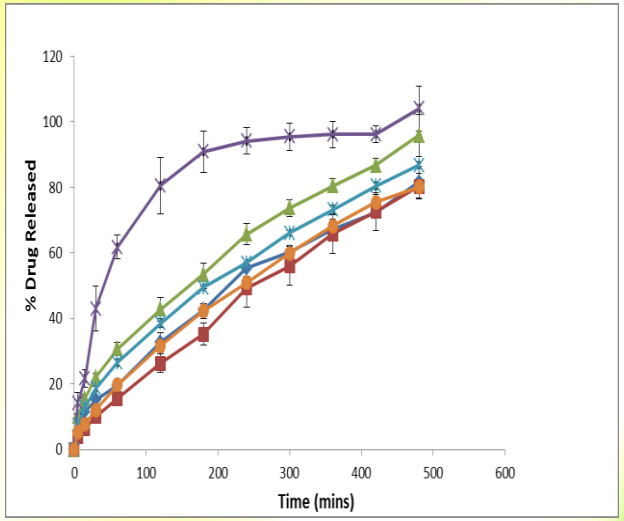
Email: amal.elkordy@sunderland.ac.uk

Floating Drug Delivery Systems with Xanthan Gum, Eudragit-RS PO or Lubritose SD: Nizatidine and Piracetam as Model Drugs

University of Sunderland







1st International Electronic Conference on Medicinal Chemistry
2-27 November 2015

sponsors: MDPI pharmaceuticals

Abstract:

Aims of the study were to prepare and investigate the dissolution and floatability profiles of Nizatidine and Piracetam effervescent floating tablets and to study the effect of Xanthan Gum, Eudragit-RS PO or Lubritose SD on tablet compression properties with or without granulation of the powder admixtures. Sodium bicarbonate was used to release CO_2 when tablets come in contact with the acidic medium. Tablets without drugs were characterised for their floatability properties in simulated gastric fluid (SGF) without enzymes at 37°C. The successful formulations regarding floatability were incorporated with Nizatidine (50mg/tablet) or Piracetam (30mg/tablet). The powder admixtures were characterised for flow properties and tablets containing drugs were evaluated via British Pharmacopeia quality control tests. All batches with Nizatidine that contain Xanthan Gum alone or in combination with Eudragit-RS PO showed good flow and compaction properties and also yielded significant ($p<0.05$) swelling and floating results. However, Piracetam batches prepared with Lubritose SD showed poor compaction, therefore granulation of the powders was applied to enhance floating tablet properties such as friability, floatability and sustainability of the drug release for more than 6 hours. **In conclusion**, Xanthan Gum and Eudragit-RS PO (used with Nizatidine) and Lubritose SD (applied with Piracetam) could be promising excipients to formulate floating tablets.

1st International Electronic Conference on Medicinal Chemistry
2-27 November 2015
sponsors: MDPI pharmaceuticals

Overview

- What are gastroretentive drug delivery systems?
- Why floating tablets
- How they can be manufactured, using model drugs
- Investigation of floating tablets
- Conclusion

University of Sunderland

Gastroretentive drug delivery systems

- To deliver oral dosage forms to the stomach and upper regions of the small intestine.
- To remain in the stomach longer than conventional dosage forms and release the drug slowly.

- To enhance bioavailability of drugs that have:

Gastroretentive drug delivery systems

University of Sunderland

- Low solubility at high pH values: Cinnarizine
- Enzymatic degradation in the intestinal or colonic environments: Antibiotics
- Short elimination half lives
- Drugs that absorb well from the stomach: Furosemide
- Local action in the stomach: antacids and drugs to treat *H. Pylori,* as an example

Advantages

- These modified dosage forms have the ability to maintain a constant level of the drug in the blood and the ability to reduce the dosing **(sustained release behavior)**
- Gastroretentive drug delivery systems overall are a very useful way of enabling a drug to be delivered to the body irrespective of the motility pattern and the different environments the drug will encounter.

Aims of the study

- To prepare and investigate the dissolution and floatability profiles of Nizatidine and Piracetam effervescent floating tablets.
- To study the effect of Xanthan Gum, Eudragit-RS PO or Lubritose SD on tablet compression properties with or without granulation of the powder admixtures.
- Lubritose SD is spray dried lactose and glyceryl monostearate; Eudragit-RS PO is a copolymer of ethyl acrylate, methyl methacrylate and a low content of methacrylic acid ester with quaternary ammonium groups.

Formulation composition of piracetam floating tablets

University of Sunderland

Ingredient / tablet (mg)	F1 25% lubritose SD	F2 40% lubritose	F3 50% lubritse SD
Piracetam	30	30	30
Lubritose SD	75	120	150
HPMC	130	85	55
Magnesium stearate	3	3	3
Sodium bicarbonate	10	10	10
Citric acid	50	50	50
Talc	2	2	2
Total Weight (mg)	300	300	300

Physical properties and quality control tests

- ✪ Weight uniformity
- ✪ Resistance to crushing
- ✪ Friability-rotation of tablets in a drum for 4 min (100 revolutions)
- ✪ Dissolution at 37°C in 0.1N HCl, 50 RPM
- ✪ Swelling test, weighing of tablets

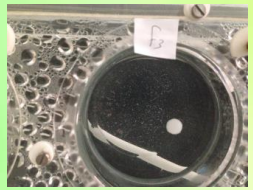
University of Sunderland

Results before granulation for piracetam

	 F1 25% Lubritose SD	 F2 40% Lubritose SD	 F3 50% Lubritose SD
Carrs index	21.21	24.32	26.67
Hardness (kg)	2.64	4.36	5.14
Friability (%)	4	7	1.5
FLT (seconds)	212	78	63
TFT (hours)	8	8	1
Swelling index (%)	233	109	-

University of Sunderland

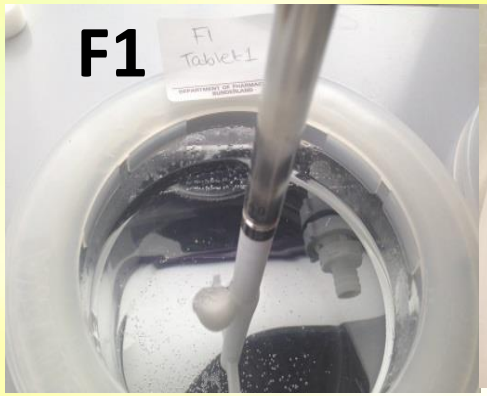
Results after granulation for piracetam

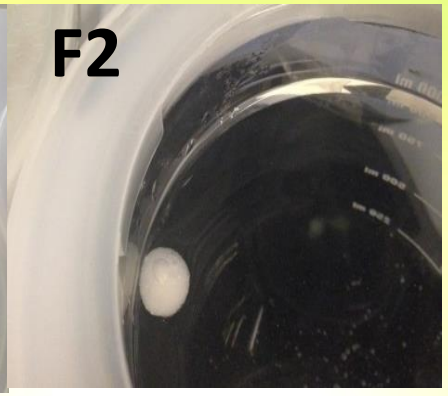


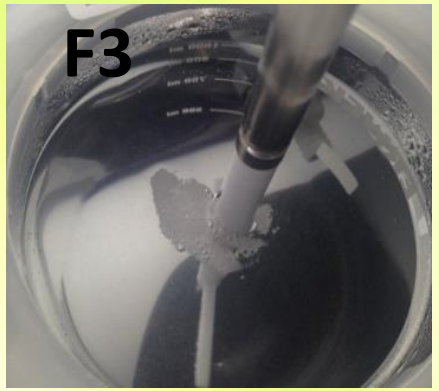
	 F1 25% Lubritose SD	 F2 40% Lubritose SD	 F3 50% Lubritose SD
Friability (%)	1	1.8	1.2
Swelling index (%)	436	333	187

University of Sunderland

Results

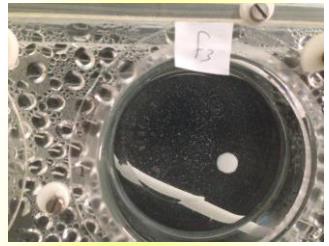


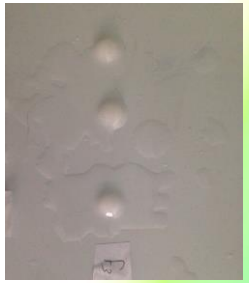




- In F1 and F2 a great deal of swelling was observed indicating the presence of the gel barrier. F3 had the least amount of HPMC hence the formation of the barrier was not as efficient as F1 and F2.

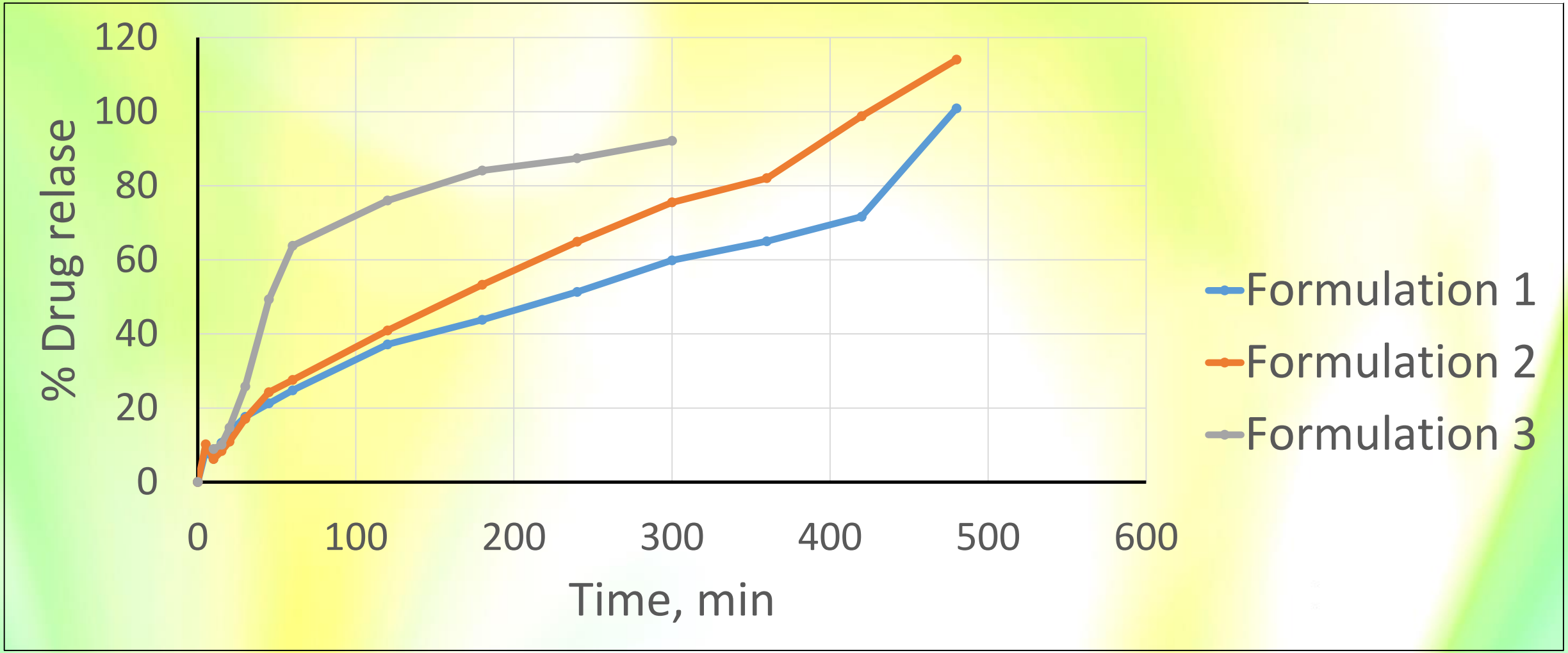
- After granulation, tablets float for more than 8 hours.





Piracetam Dissolution

University of Sunderland



Drug Dissolution for Piracetam

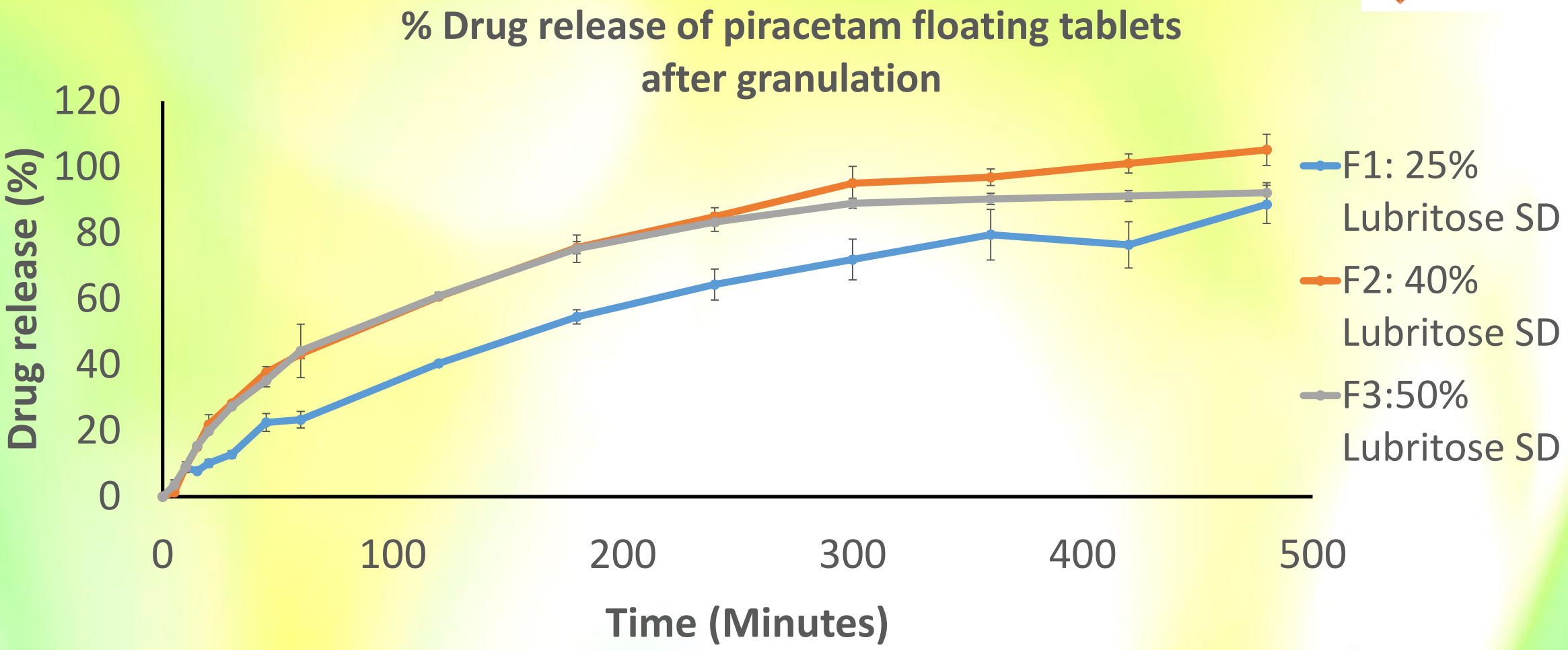
University of Sunderland

- The drug release in F1 and F2 was more gradual over time as there was more of the polymer present which controlled the rate at which the drug was released. F3 had the least amount of HPMC hence the formation of the barrier was not as efficient as F1 and F2 causing the drug release from F3 to be faster over time. Less HPMC present meant the gel barrier was weak and the tablet was easily penetrated by the fluids, thus the drug dissolution process was faster.

- Lubritose SD did not directly affect the floating properties of the tablets however differences were seen in the flow properties. Increased lubritose SD led to an increase in the tablet hardness and a decrease in lag time. Granulation of Lubritose SD containing tablets improved friability and floating duration.

Drug Dissolution

University of Sunderland



Formulation composition of Nizatidine (50mg) floating tablets

University of Sunderland

Formula (mg)	HP MC	Sodium Alginate	Xanthan Gum	Sodium Bicarbonate	Magnesium Stearate	Citric Acid	Povidone	Lactose	Eudragit RS PO
F1	150	--------	--------	135	9	-----	45	--------	---------
F2	-----	--------	165	150	9	20	30	65	---------
F3	Same As F2 Just Increased Compression Force								
F4	------	--------	120	110	3	15	20	45	-------
F5	Same As F1 Just Increased Compression force								
F6	-------	---------	140	45	9	10	30	65	140

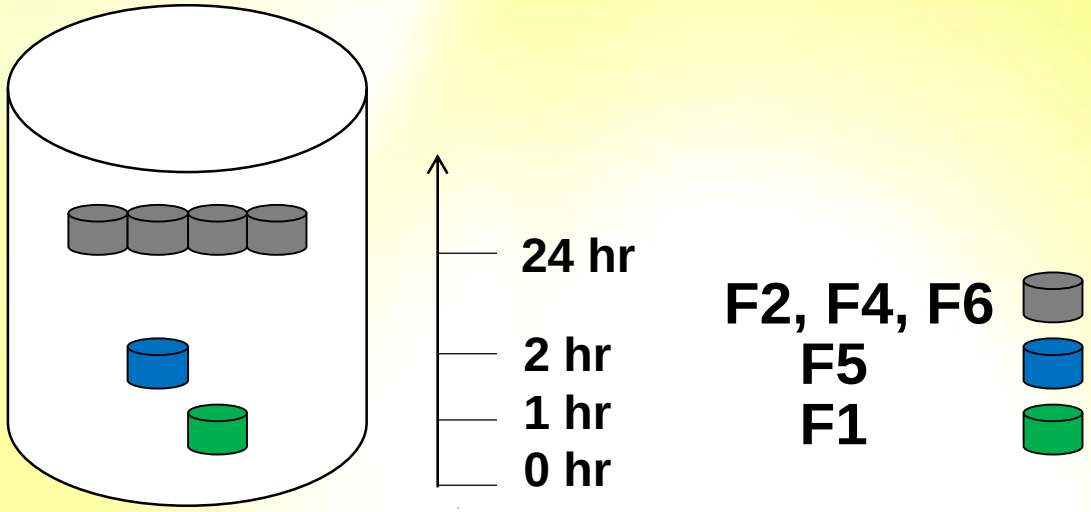
Formulation of Nizatidine (50mg) floating tablets

University of Sunderland

All batches (F1-F6) with Nizatidine that contain Xanthan Gum alone or in combination with Eudragit-RS PO showed good flow and compaction properties and also yielded significant ($p<0.05$) swelling and floating results.

The drug content of all formulations ranged from 101.7-107.9%. F1-F6 complied with the British pharmacopoeia specifications regarding friability and weight uniformity. Tablet hardness was within acceptable range (45-57N).

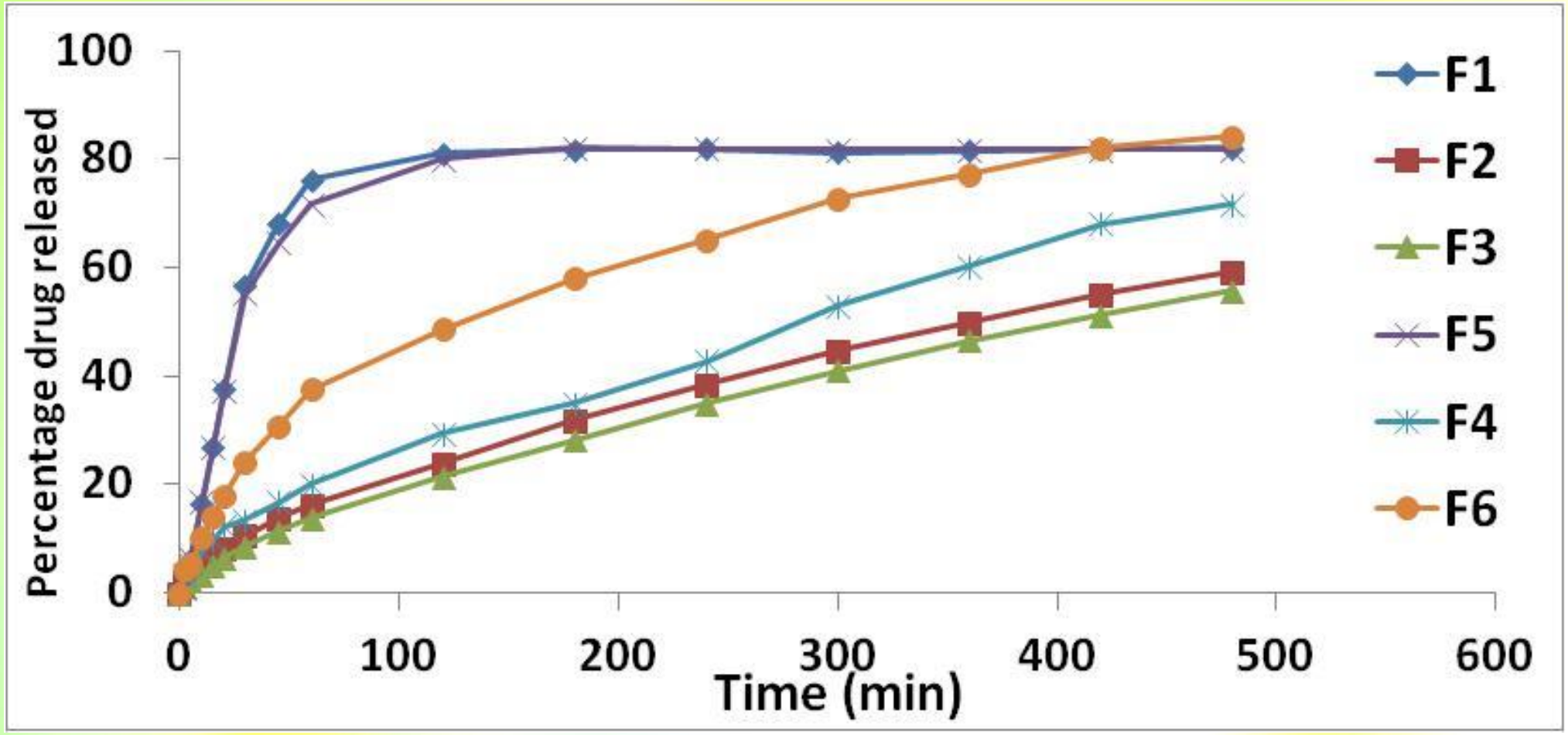
Formulation of Nizatidine (50mg) floating tablets



Duration of floating of Nizatidine formulations

University of Sunderland

Dissolution data of Nizatidine floating formulations



University of Sunderland

Conclusion

❖ In conclusion, Xanthan Gum and Eudragit-RS PO (used with Nizatidine) and Lubritose SD (applied with Piracetam) could be promising excipients to formulate floating tablets.

❖ Granulation of piracetam formulation (with 50% Lubritose SD) enhanced the floating properties and also drug release was sustained.