



**Faculty of Graduate Studies
Applied and Industrial Technology Program**

**Determination and evaluation of stability
of Extemporaneous preparations**

**Supervised by :
Dr. Tareq Jubeh**

**Prepared by :
Anwar Abu Sneineh**



Introduction :

- A lack of commercially available oral liquids creates a problem to health care professionals especially the pharmacist when it is required to prepare a stable and homogeneous extemporaneous preparation

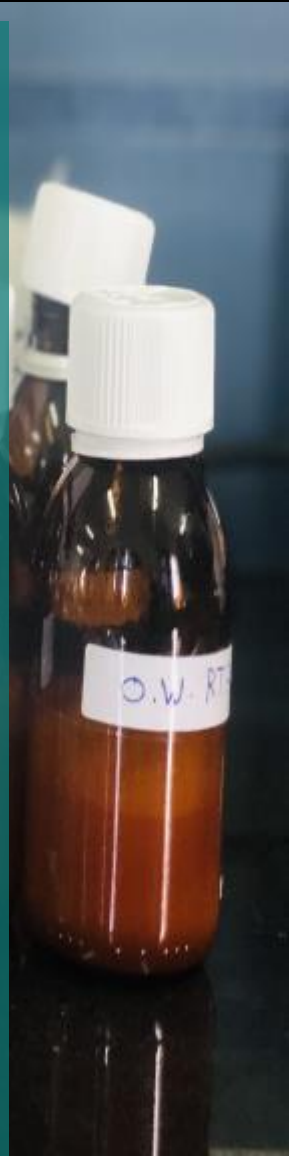
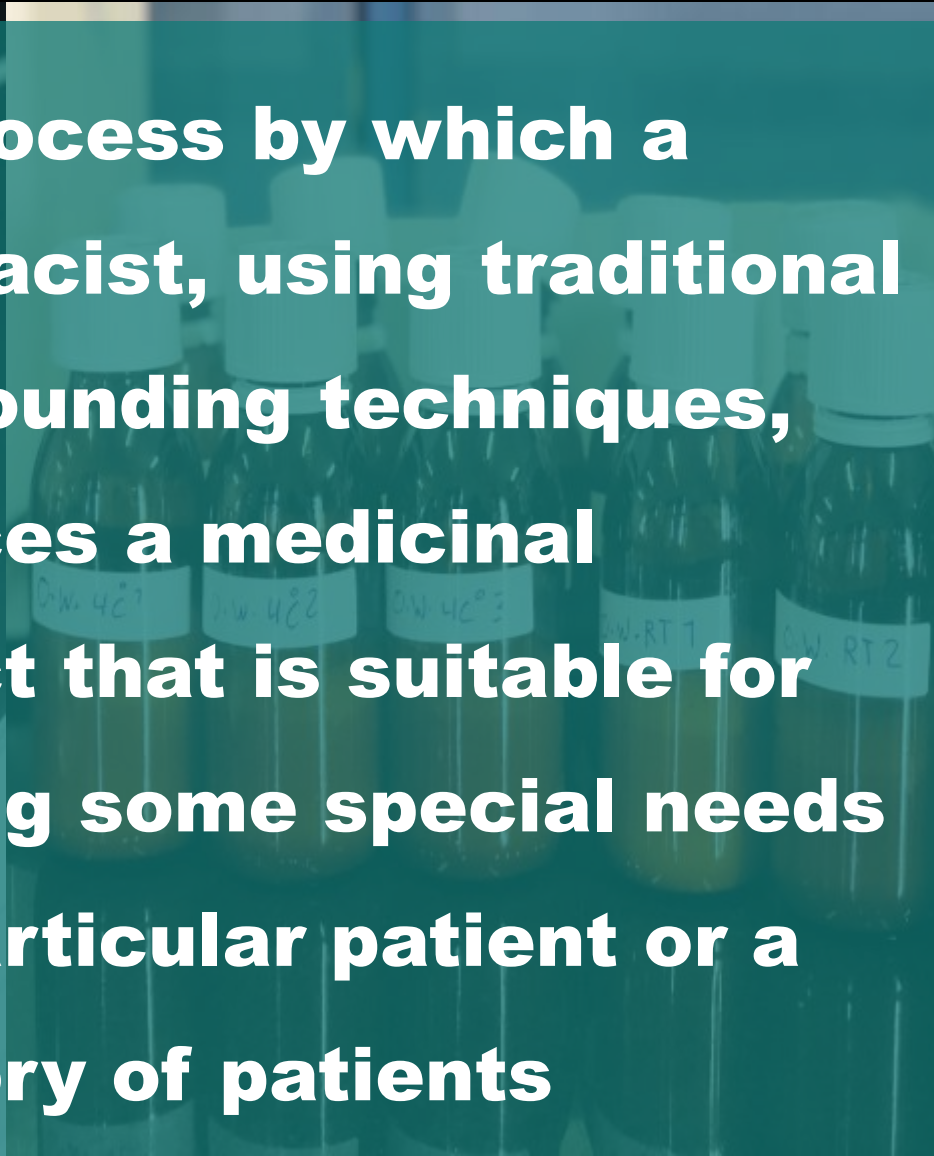



Introduction

Extemporaneous compounding is necessary to provide health care to populations of patients such as geriatrics, pediatric patients and other adults who are not able to swallow solid dosage forms due to swallowing difficulties.

What is extemporaneous preparation ?

The process by which a pharmacist, using traditional compounding techniques, produces a medicinal product that is suitable for fulfilling some special needs of a particular patient or a category of patients





Examples of drugs prepared in the local market as extemporaneous liquids :

- pantoprazole
- Captopril
- Aspirin
- Spironolactone
- Furosemide
- Amlodipine
- Amiodarone
- Hydrochlorothiazide
- Omeprazole
- Midazolam
- Enalapril
- Propranolol
- Folic acid



How do Pharmacists prepare oral liquids using tablets as starting materials?

- 1- Grinding and adding water (sometimes with flavor and sweetening)**
- 2- Adding simple syrup**
- 3- Using a suspending agent**

Problems and aims of concern in extemporaneously prepared drug

Chemical, physical and microbiological stability data, short shelf-life

Published standards

Various publications

Proof of dose uniformity

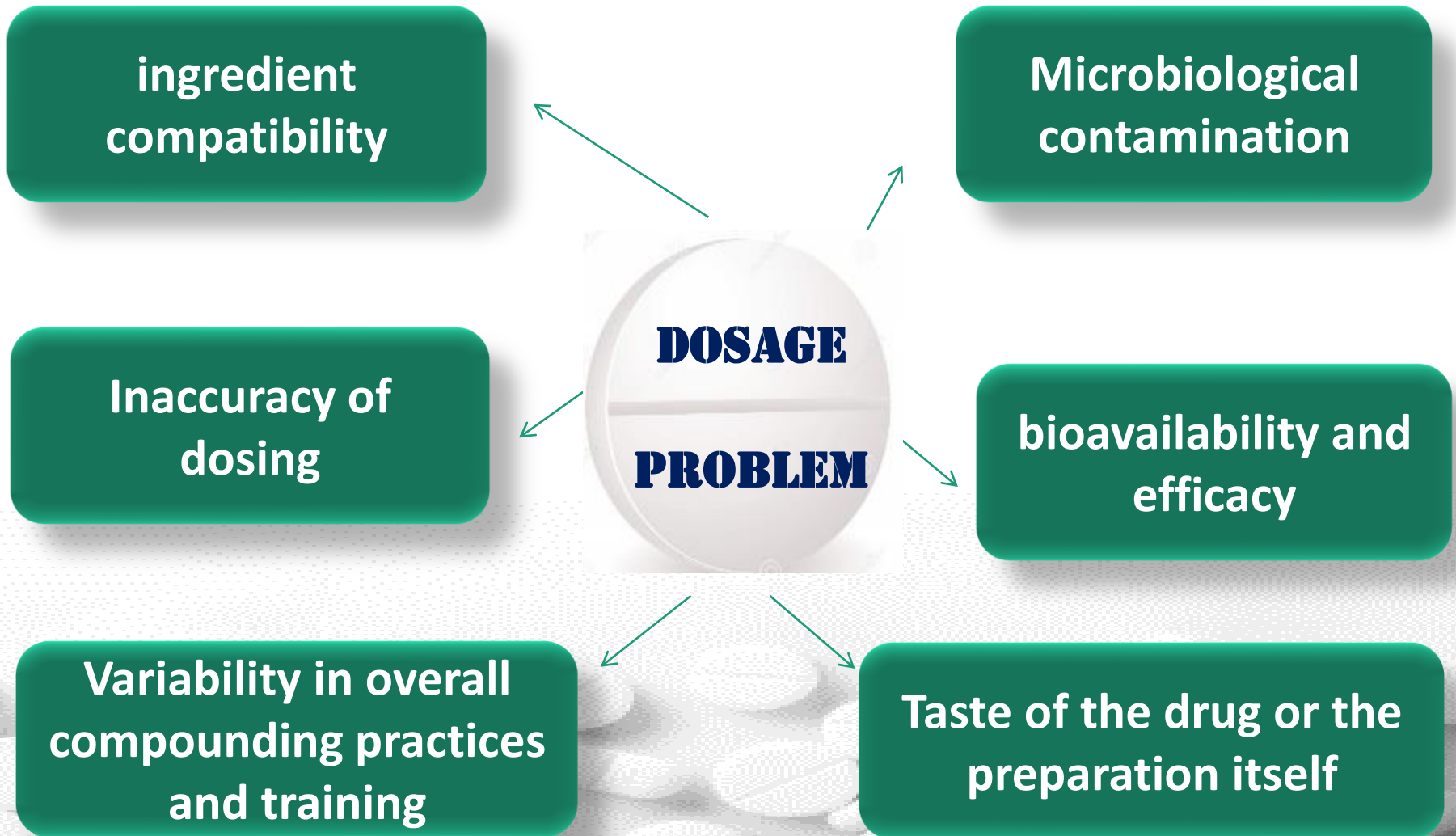
Adequate dosage form

Information about validation and reproducibility



**LACK
OF**

Problems and aims of concern in extemporaneously prepared drug,,,





Problem statement :

- The stability and homogeneity of extemporaneous preparations in the local Palestinian pharmacy sector are questionable.
- Many question marks are raised towards the way these preparations are made and the preformulation steps taken prior to their compounding .
- **It is vital to take into account the physicochemical properties of the drug.**



Problem statement

- The final product will be missing fundamental elements such as uniformity of dose, stability and organoleptic properties.
- Moreover, it is well known that active pharmaceutical materials differ in their solubilities, pKa, physical form, taste, etc.



Objectives

1

study the dose uniformity and stability of extemporaneous preparations (of furosemide, Pantoprazole).

2

To prepare oral liquid dosage forms containing furosemide and pantoprazole, based on the formulative procedures applied in pharmacies .

3

To test the stability (by measuring the concentration of active material, dose uniformity



Chosen drugs



A. Furosemide

- It is a sulfonamide, a chlorobenzoic acid and a member of furans. It is a potent loop diuretic, widely used to treat hypertension and edema.
- It is partially insoluble in water Slightly soluble in chloroform, ether, Soluble in acetone, methanol, DMF, and aqueous solutions above pH 8.0.



B. Pantoprazole :

- **Pantoprazole sodium** is a first-generation proton pump inhibitor (PPI) used for the management of (GERD), for gastric protection to prevent recurrence of stomach ulcers or gastric damage from chronic use of NSAIDs , and in the treatment of H. pylori infections.
- **Pantoprazole sodium** is freely soluble in water

Methods

Part (1) : Preparation and testing of Furosemide and pantoprazole Suspensions

A) With D.W



Rt 1

Rt 2

Rt 3



4c1

4c2

4c3



× 12 P

× 10 F



DISTILLED WATER





1 ML



250 ml



B) With simple syrup 85%



X 12 P

X 10 F



SYRUP



Rt 1



Rt2



Rt3



4c1



4c2



4c3





1 ML



250 ml



C) Pantoprazole and furosemide susp. with suspending agents (Xanthan gum , carboxymethyl cellulose)



XANTHAN GUM (0.2G/100ml /0.5G/100ML)
CMC 0.2G/100ML

20 MIN



120 ML SYURP

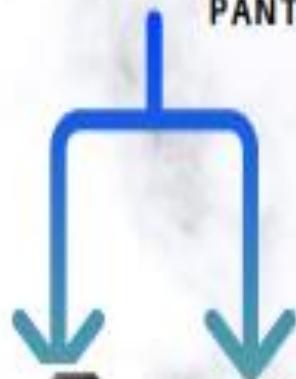


DISTILLED WATER UP TO 300 ML

PANTOPRAZOLE/ FUROSEMIDE & XANTHAN SUSP



PANTOPRAZOLE / FUROSEMIDE & CMC SUSP



RT1 RT2 RT3

4C1 4C2 4C3

RT1 RT2 RT3

4C1 4C2 4C3



1 ML



250 ml

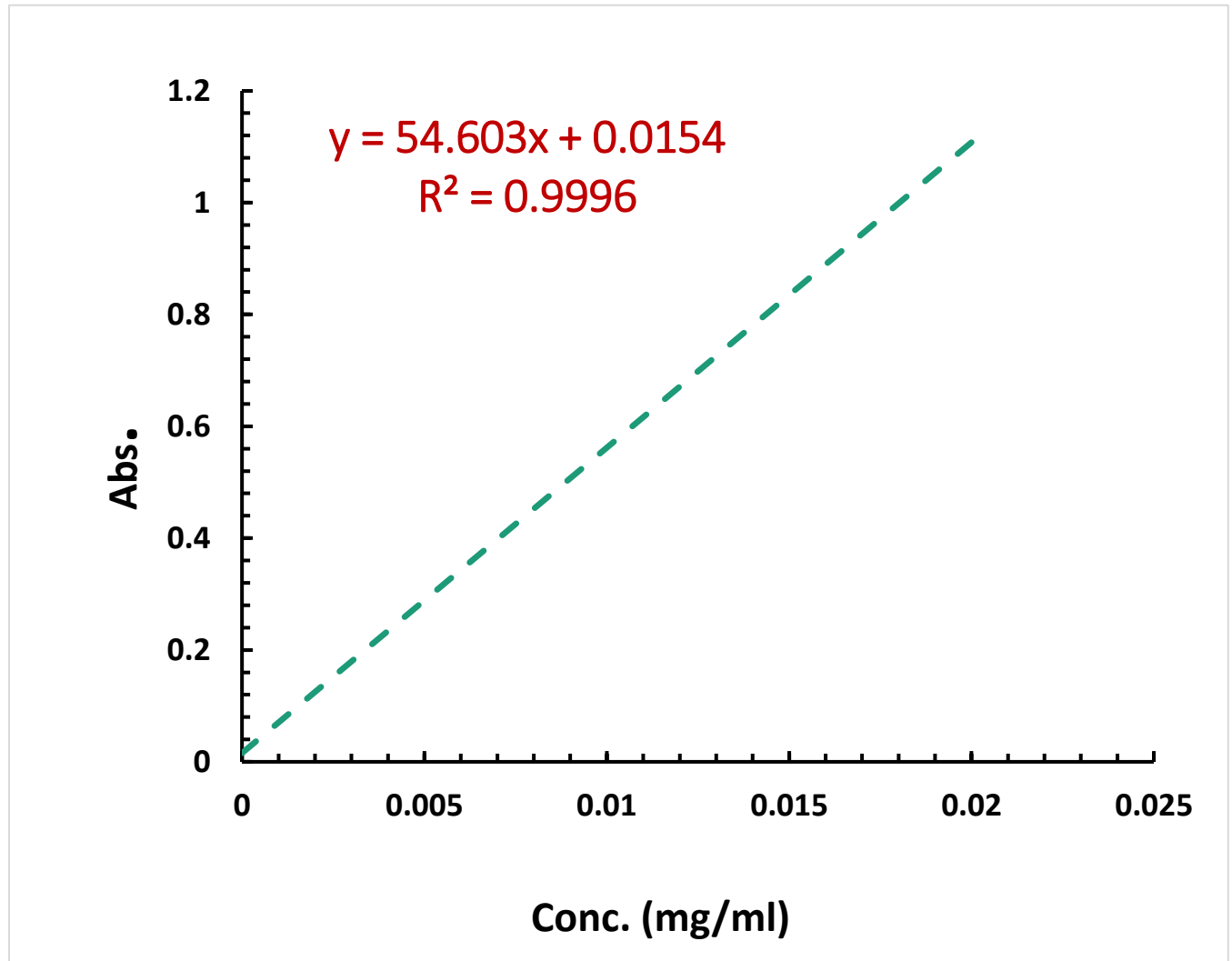


RESULTS AND DISCUSSION



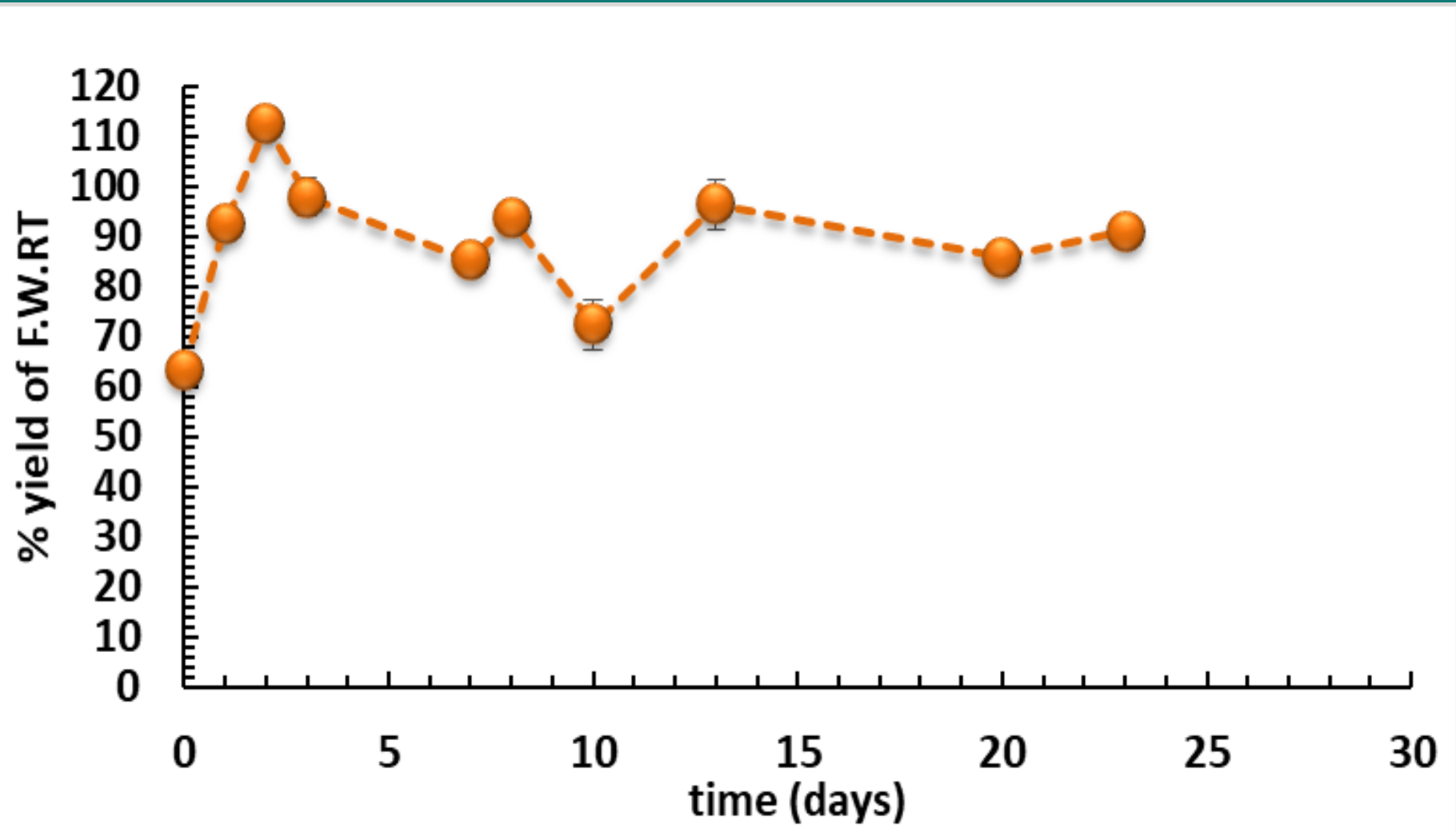
A. Sample analysis of furosemide suspensions:

Conc.	UV Abs.
0	0
0.02	1.107
0.004	0.235
0.0008	0.063
0.00016	0.035



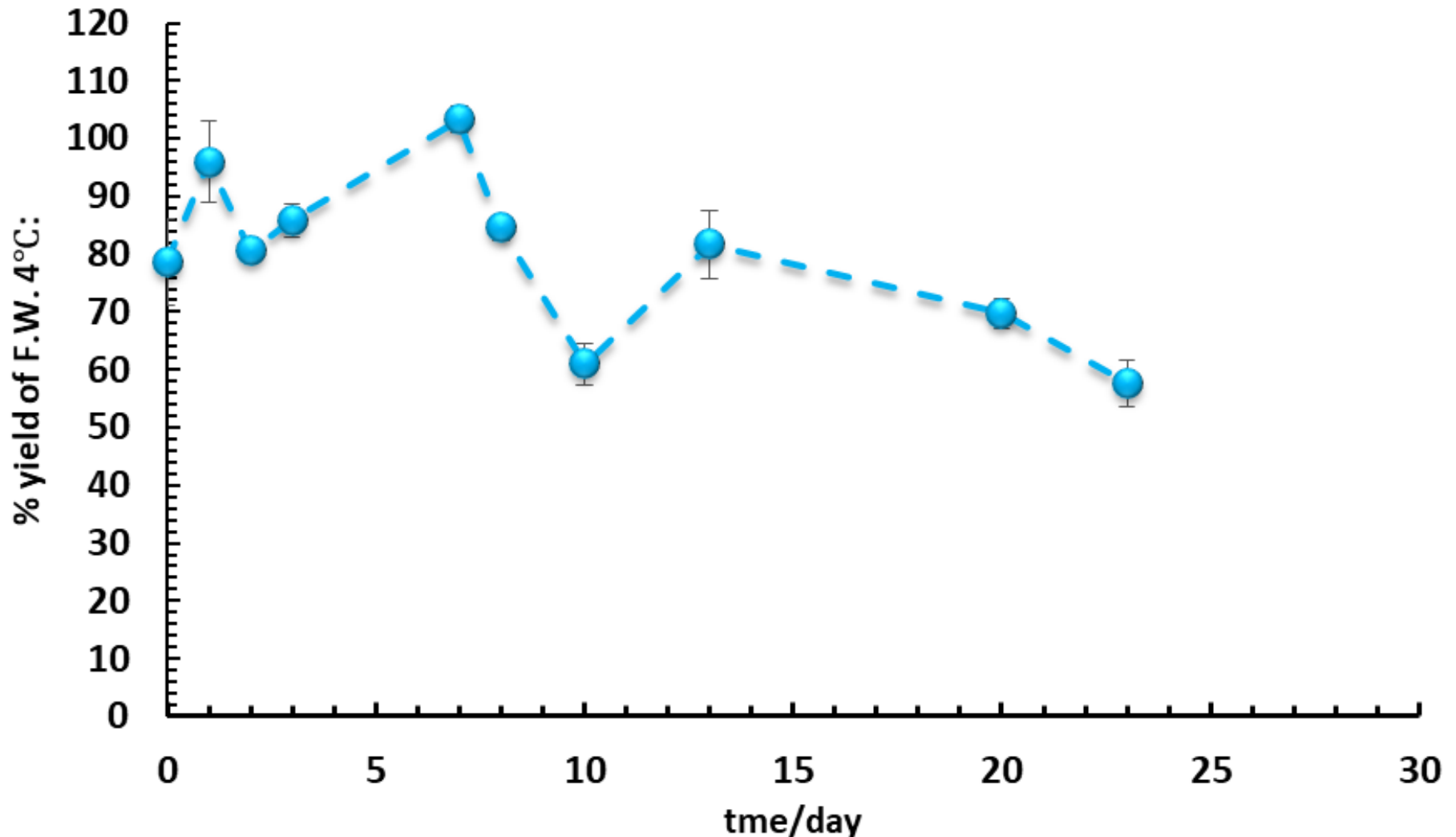
Calibration curve of furosemide

Furosemide suspension in water at room temperature:



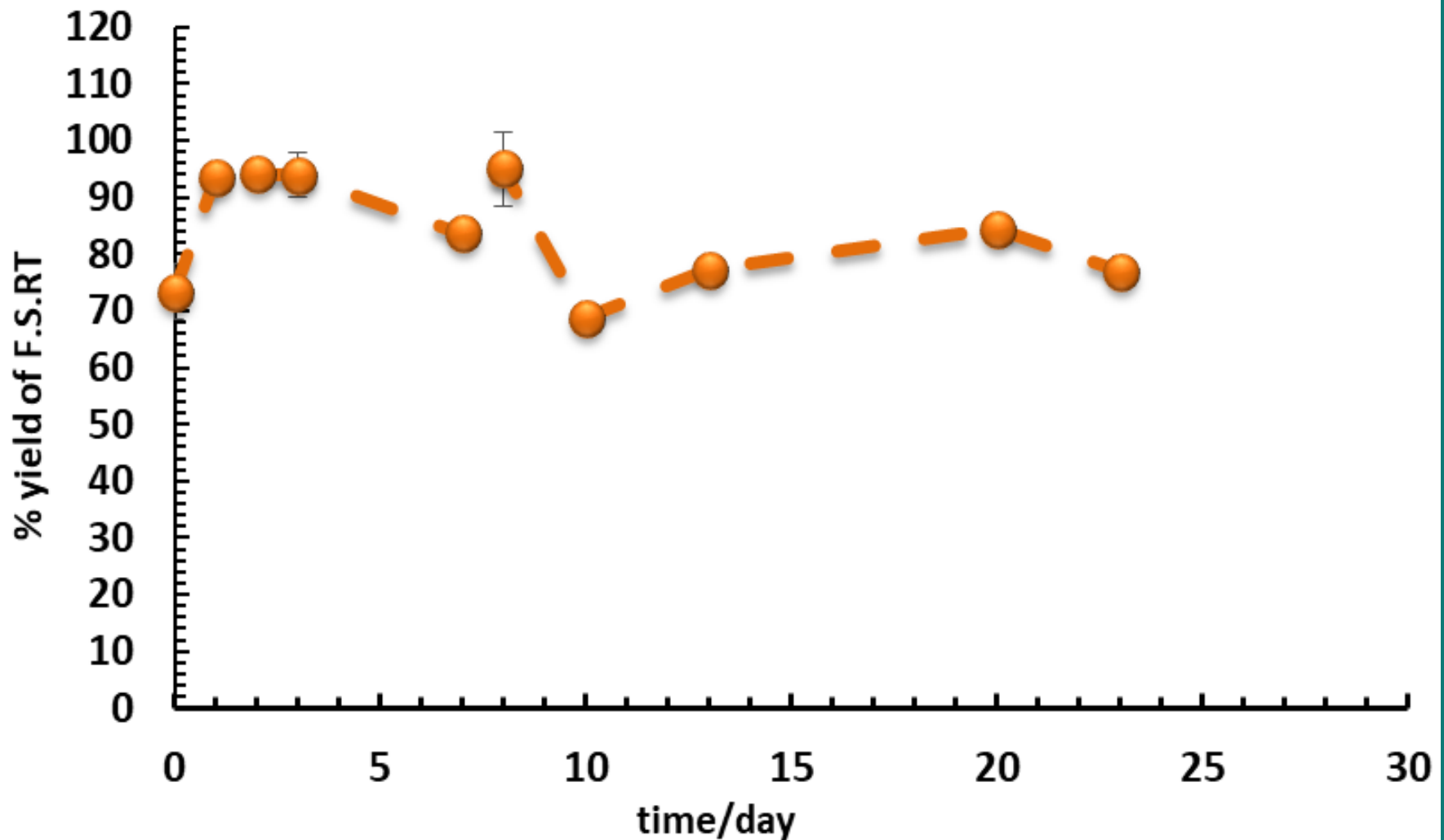
Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in water and preserved for the duration of the study at room temperature

Furosemide suspension in water at 4°C:



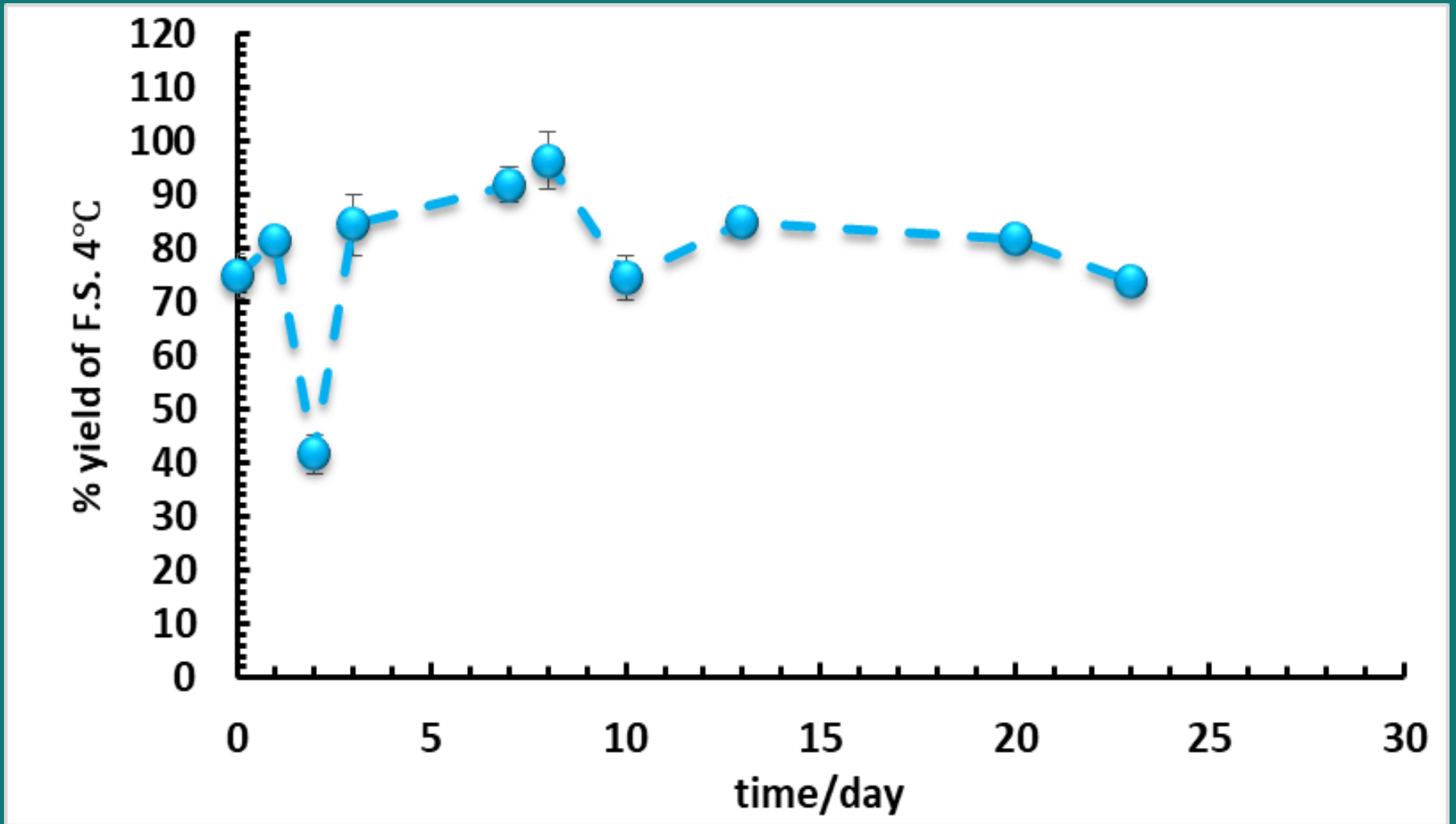
Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in water and preserved for the duration of the study at 4°C

Furosemide suspension syrup at Room temperature:



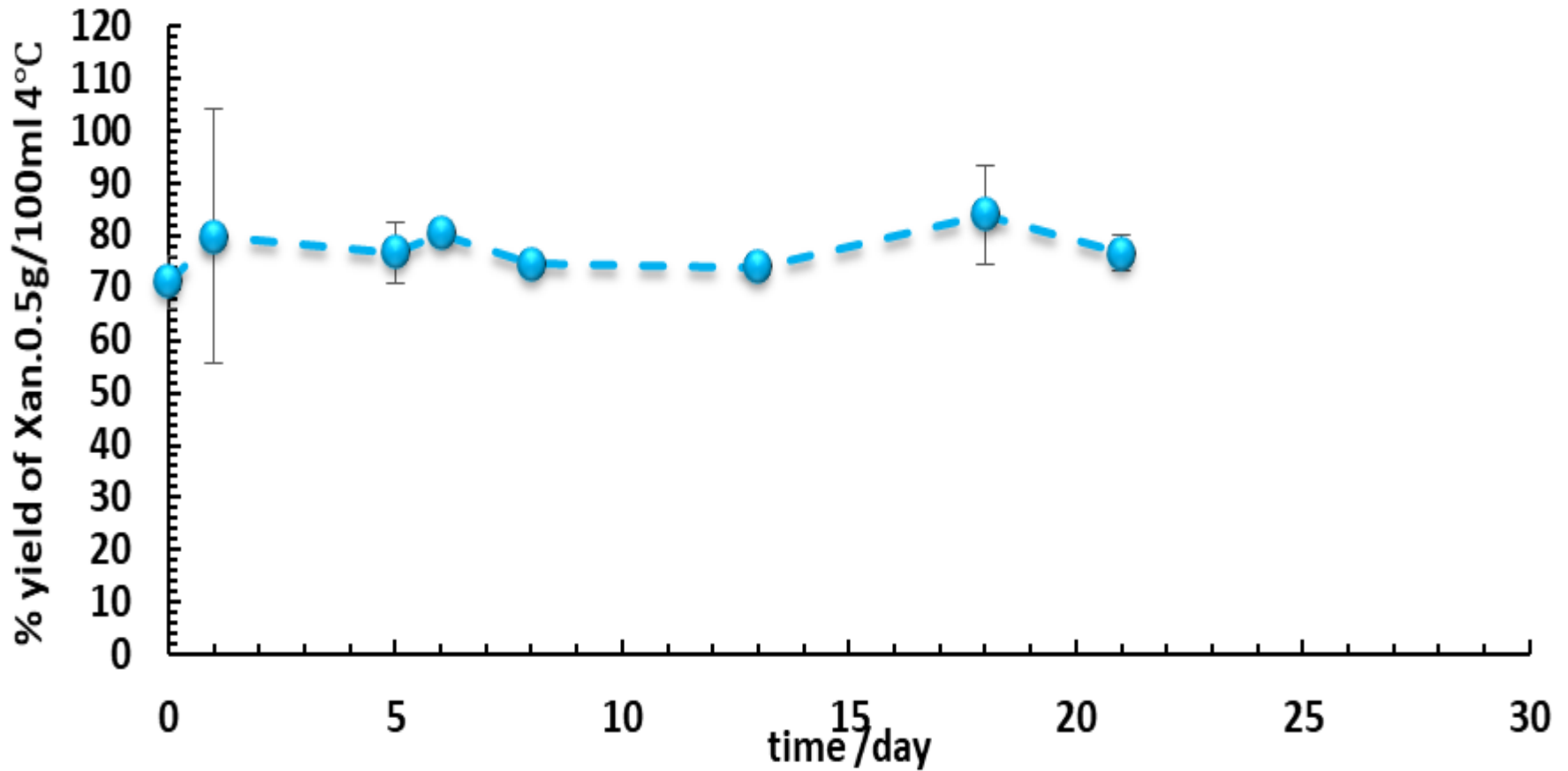
Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in syrup and preserved for the duration of the study at R.T

Furosemide suspension syrup at 4°C:



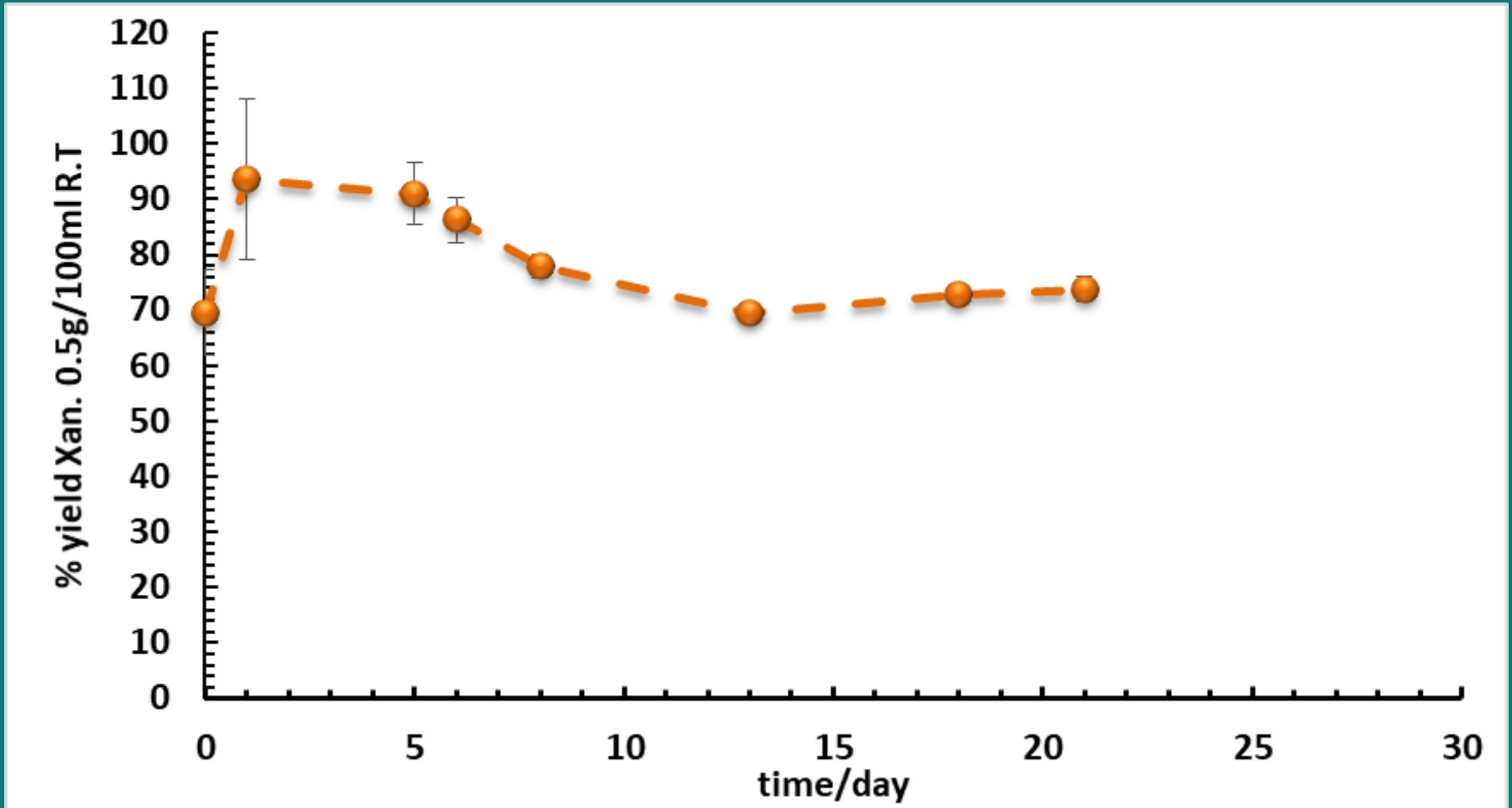
Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in syrup and preserved for the duration of the study at 4°C

Furosemide suspension in syrup using Xanthan gum 0.5g/100ml at 4°C:



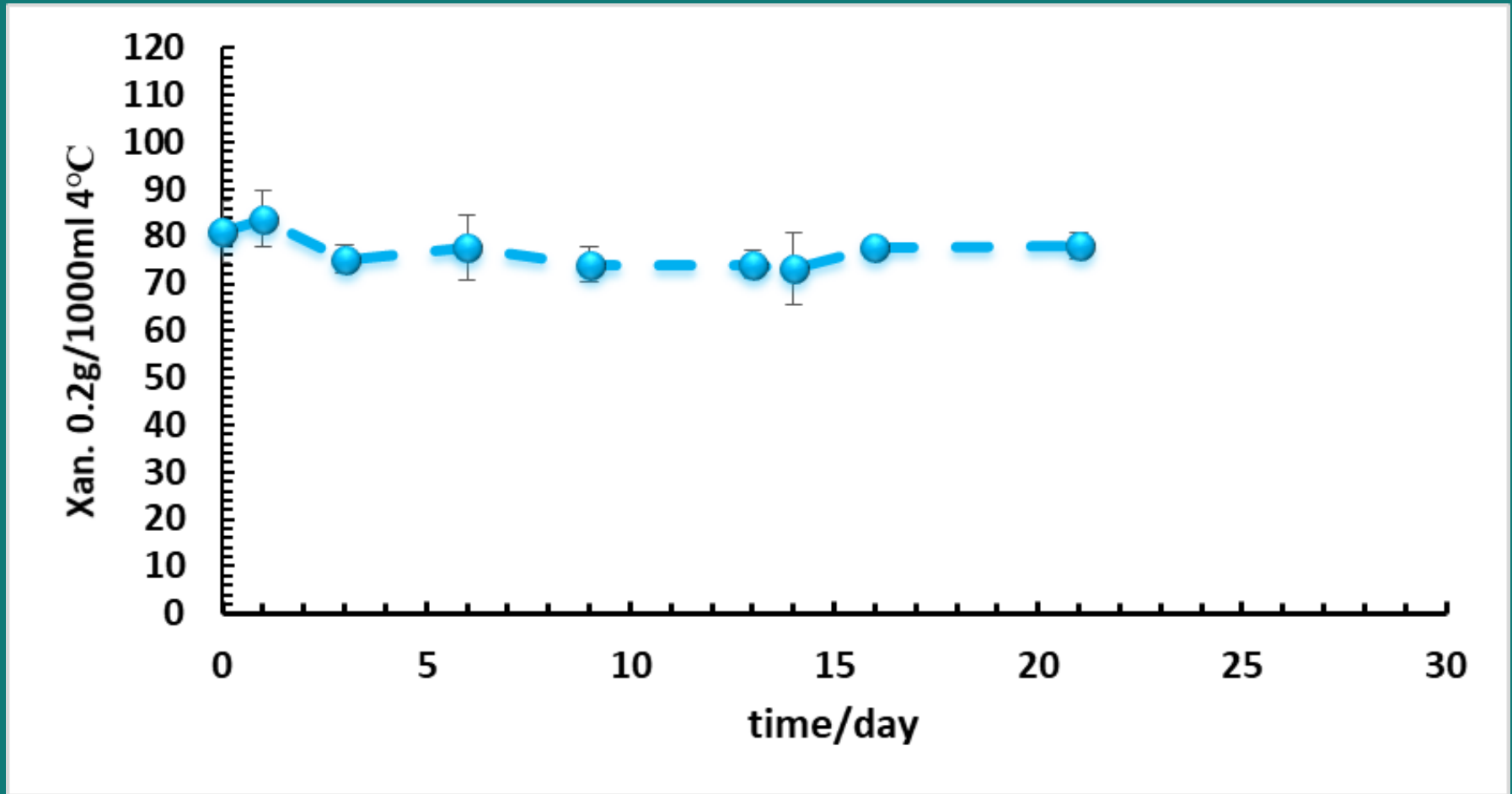
Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in xanthan gum 0.5g/100ml suspension and preserved for the duration of the study at 4°C

Furosemide suspension in syrup using Xanthan gum 0.5g/100ml at R.T:



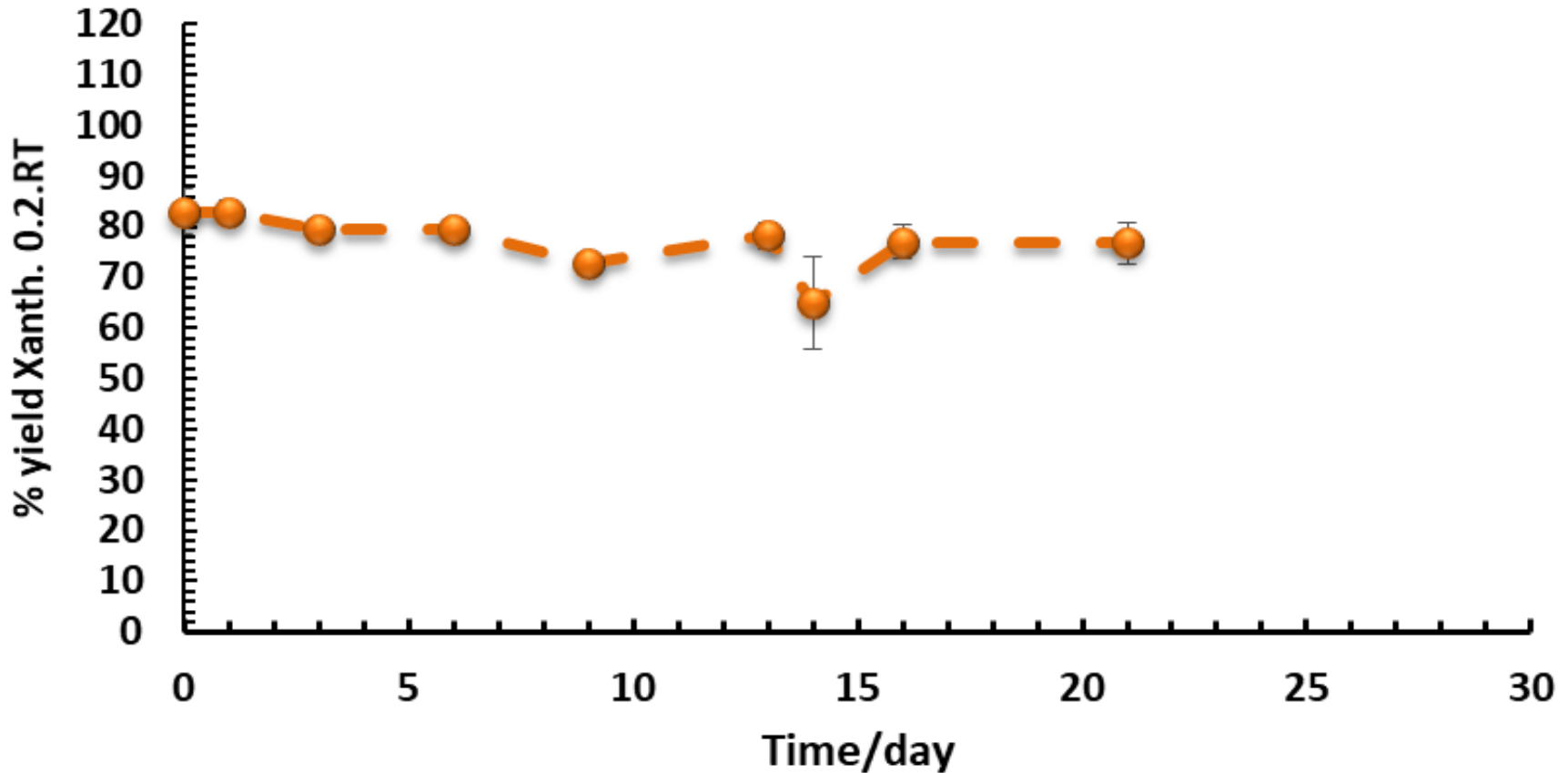
Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in xanthan gum 0.5g/100ml suspension and preserved for the duration of the study at R.T

Furosemide suspension in syrup using Xanthan gum 0.2g/100ml at 4°C:



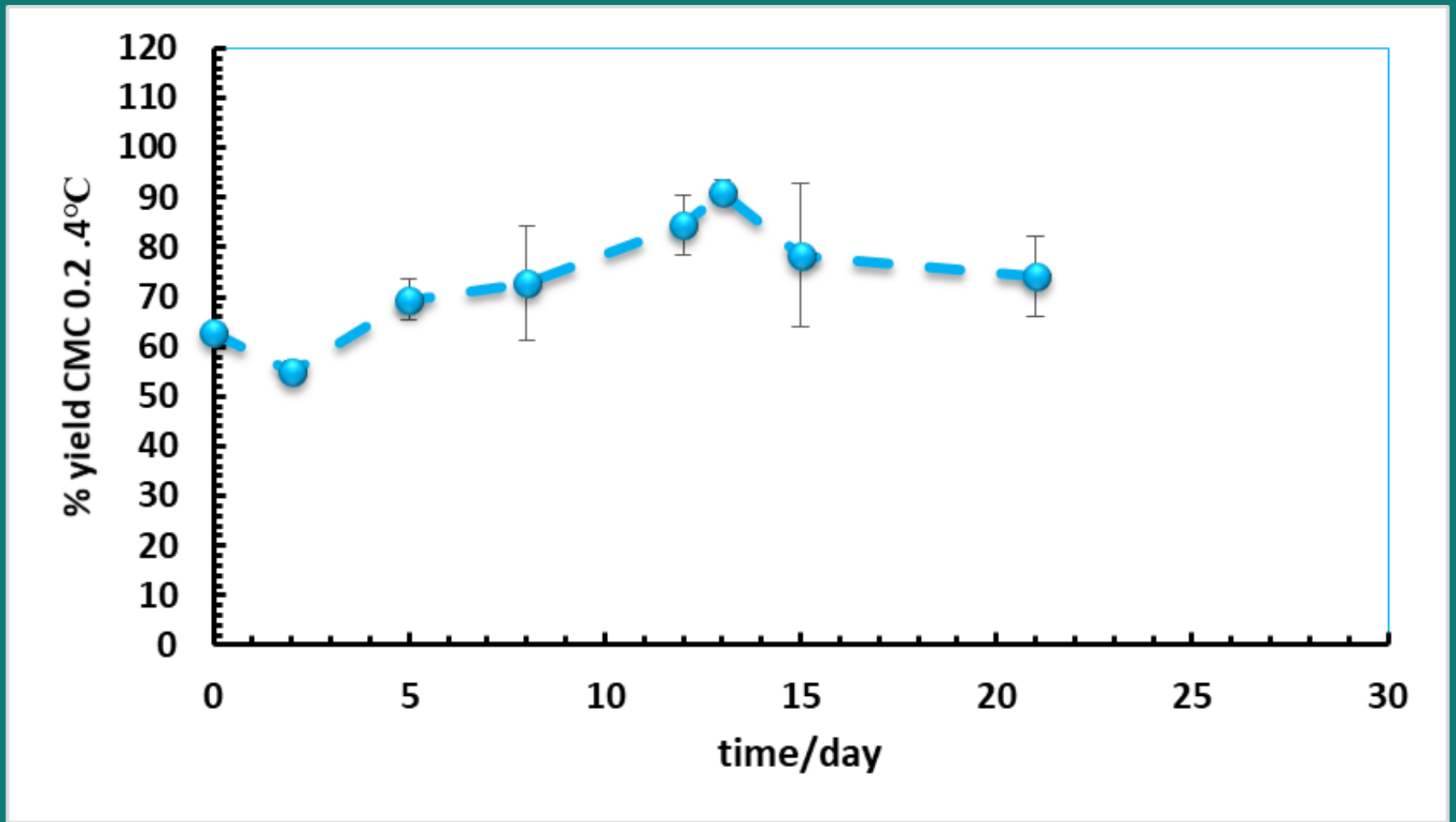
Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in xanthan gum 0.2g/100ml suspension and preserved for the duration of the study at 4°C

Furosemide suspension in syrup using Xanthan gum 0.2g/100ml at R.T:



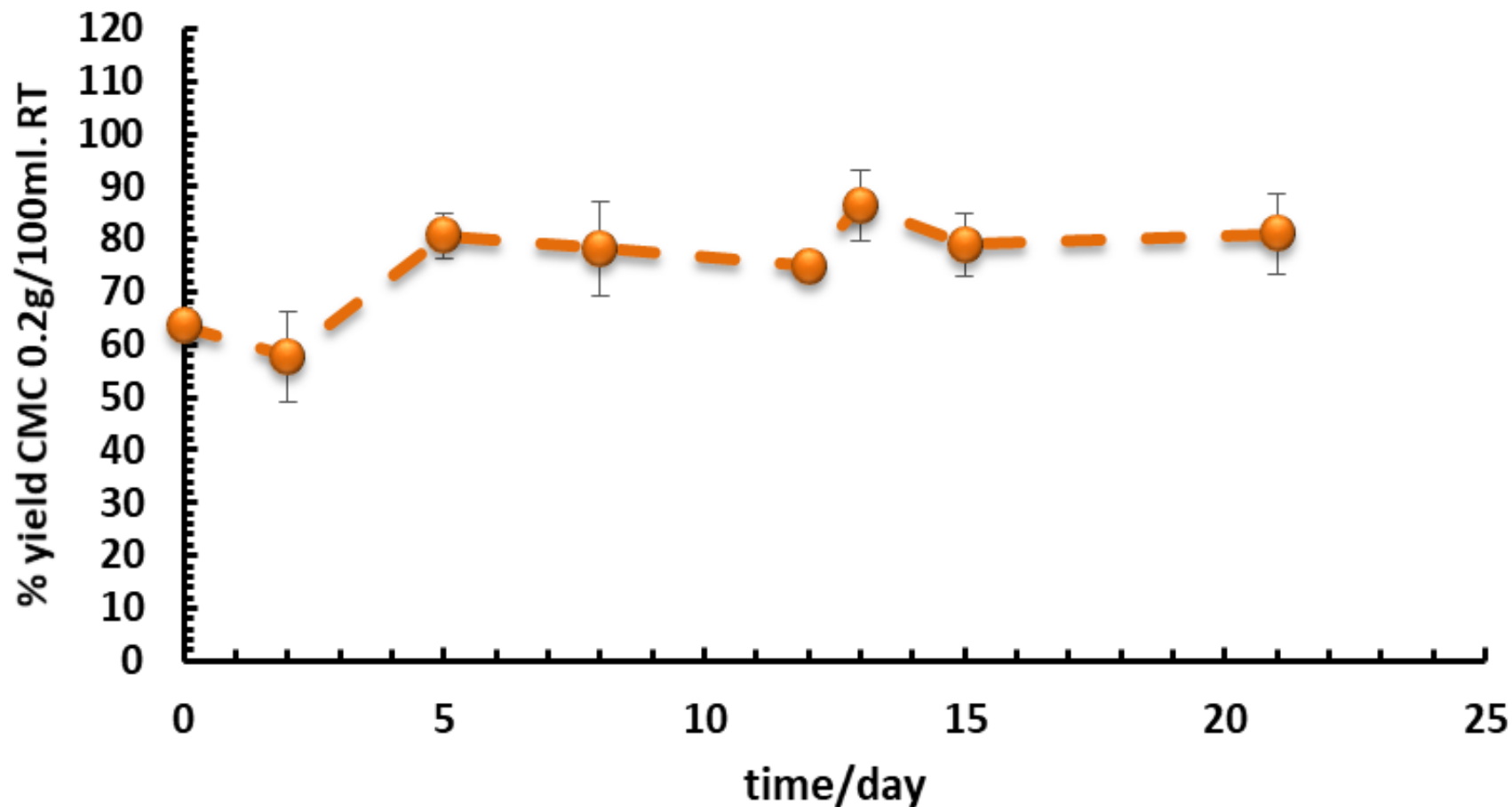
Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in xanthan gum 0.2g/100ml suspension and preserved for the duration of the study at R.T

Furosemide suspension in syrup using CMC.0.2g/100ml at 4°C:



Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in CMC 0.2g/100ml suspension and preserved for the duration of the study at 4°C

Furosemide suspension in syrup using CMC.0.2mg/100ml at RT:

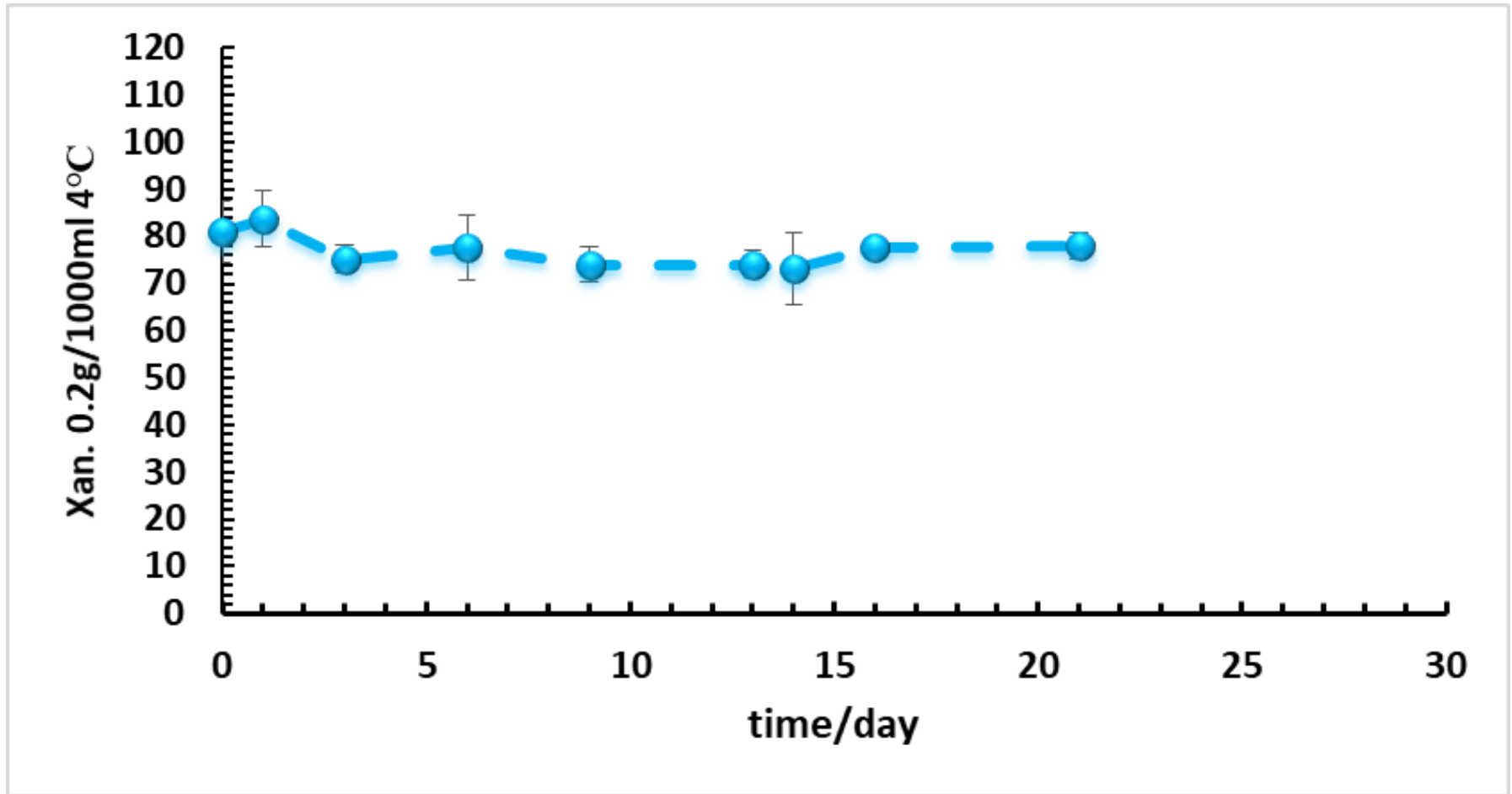


Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in CMC 0.2g/100ml suspension and preserved for the duration of the study at R.T

A summary of the “range” of the different preparations

Preparation	Range
Furosemide in water at RT	45.8
Furosemide in water at 4C	45.6
Furosemide in syrup at RT	26
Furosemide in syrup at 4C	50
Furosemide Suspension with 0.5% xanthan gum at RT	25.1
Furosemide Suspension with 0.5% xanthan gum at 4C	13
Furosemide Suspension with 0.2% xanthan gum at RT	10.7
Furosemide Suspension with 0.2% xanthan gum at 4C	18
Furosemide Suspension with 0.2% CMC at 4C	36
Furosemide Suspension with 0.2% CMC at RT	23.3

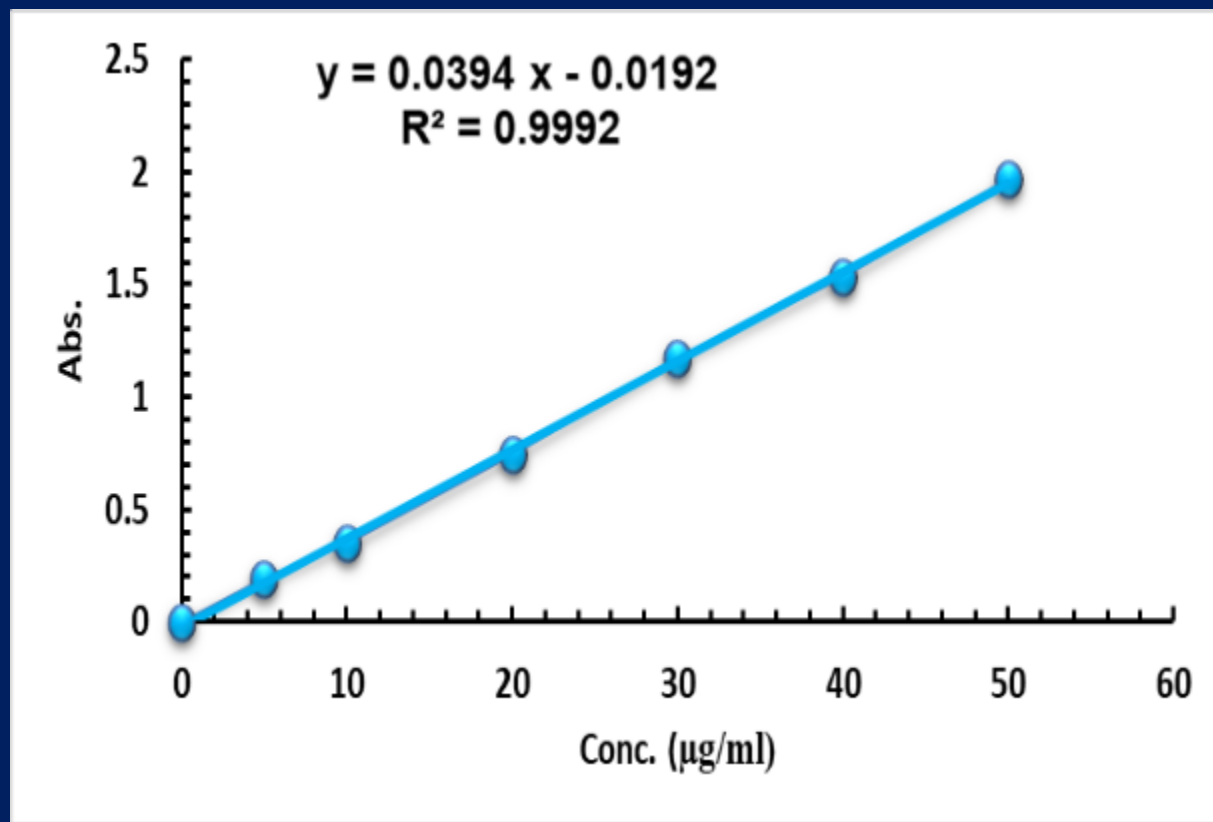
Best formulation in terms of homogeneity, range =10



Percentage yield (actual/expected X100%) of samples taken from Furosemide tablets dispersed in xanthan gum 0.2g/100ml suspension and preserved for the duration of the study at 4°C

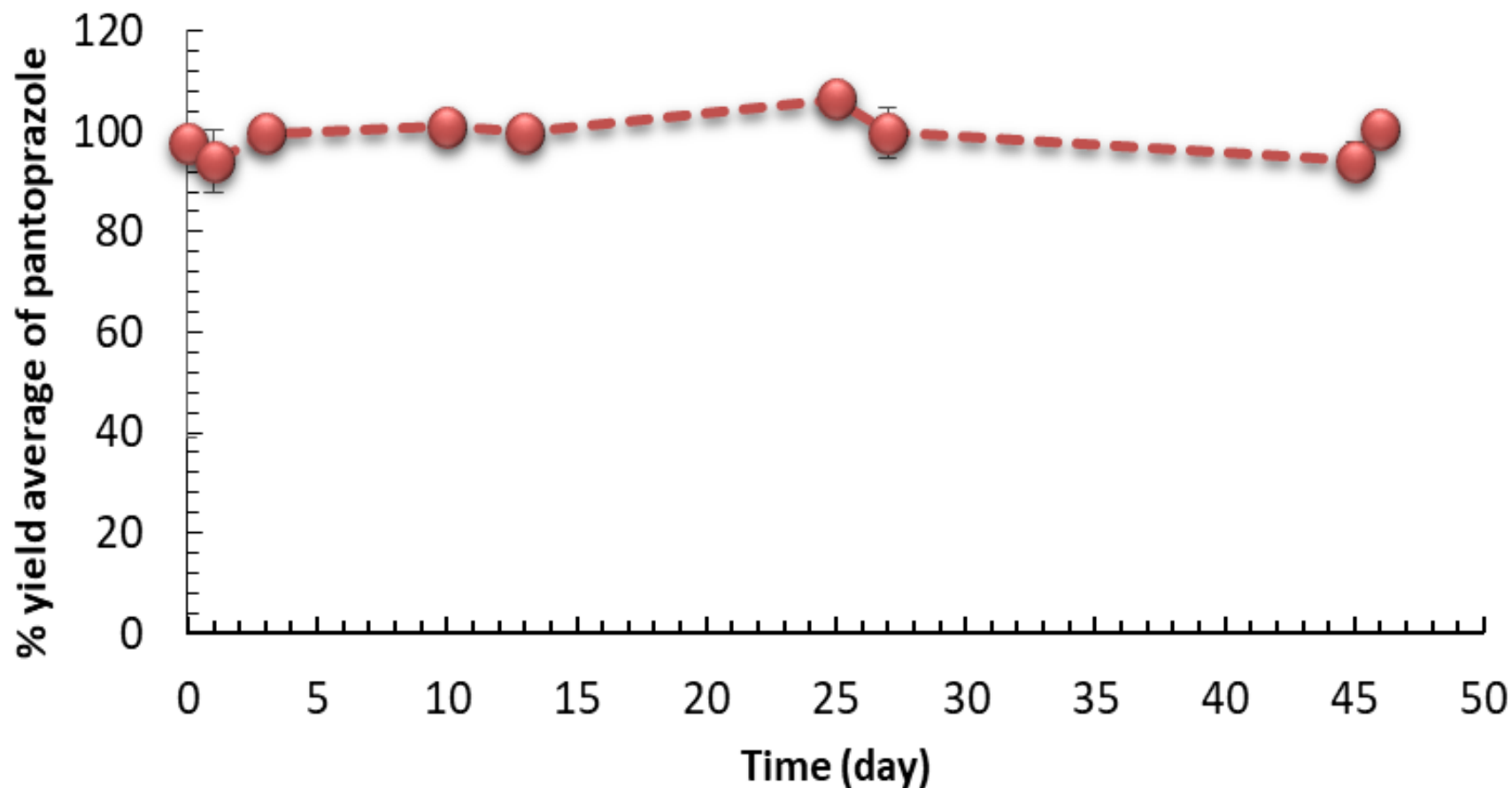
B. Pantoprazole analysis:

Conc. (µg)	Conc. (mg)	Abs.
0	0	0
5	0.005	0.192
10	0.01	0.354
20	0.02	0.741
30	0.03	1.172
40	0.04	1.537
50	0.05	1.971



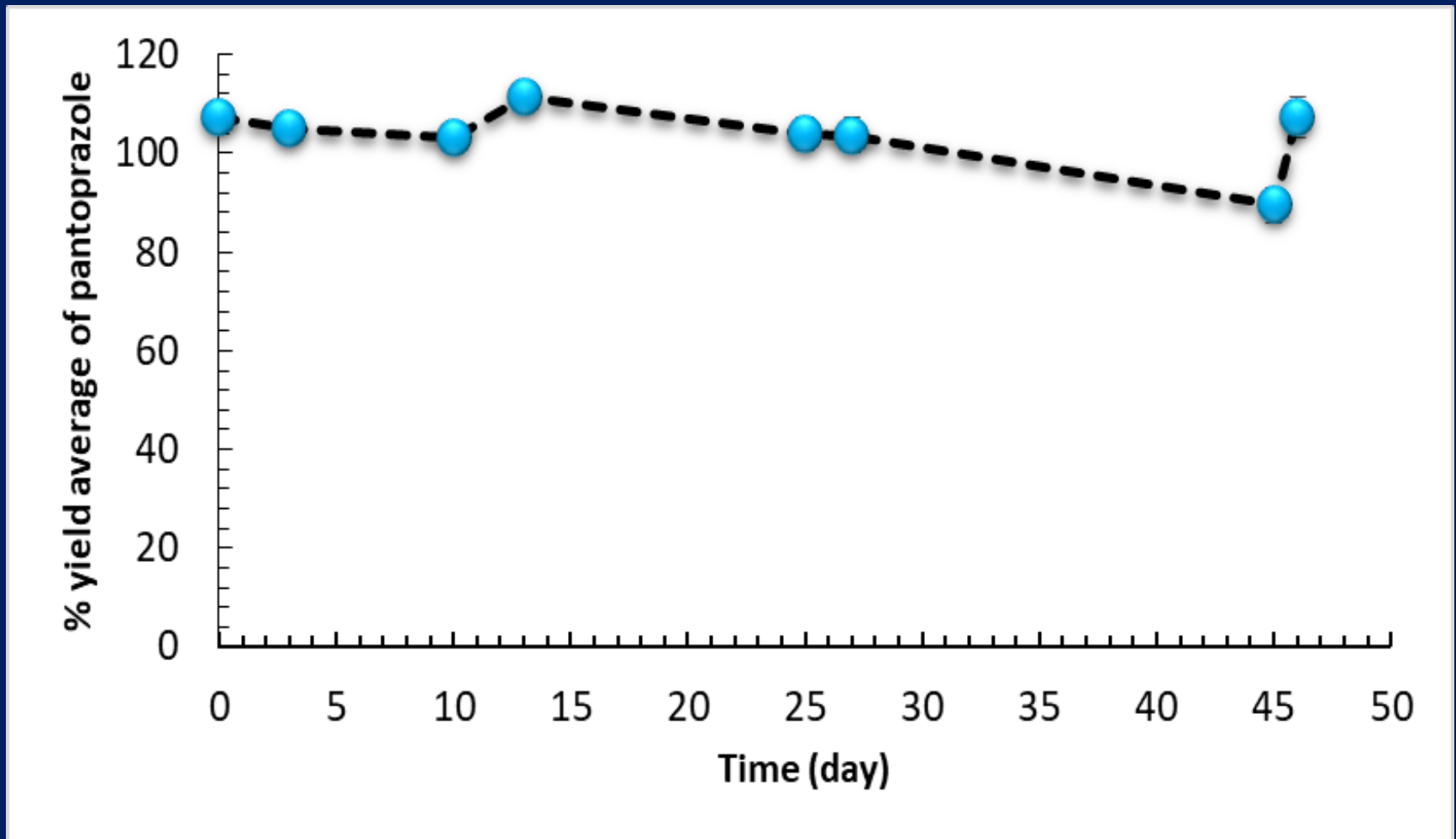
Calibration Curve of Pantoprazole

Pantoprazole suspension in water at RT:



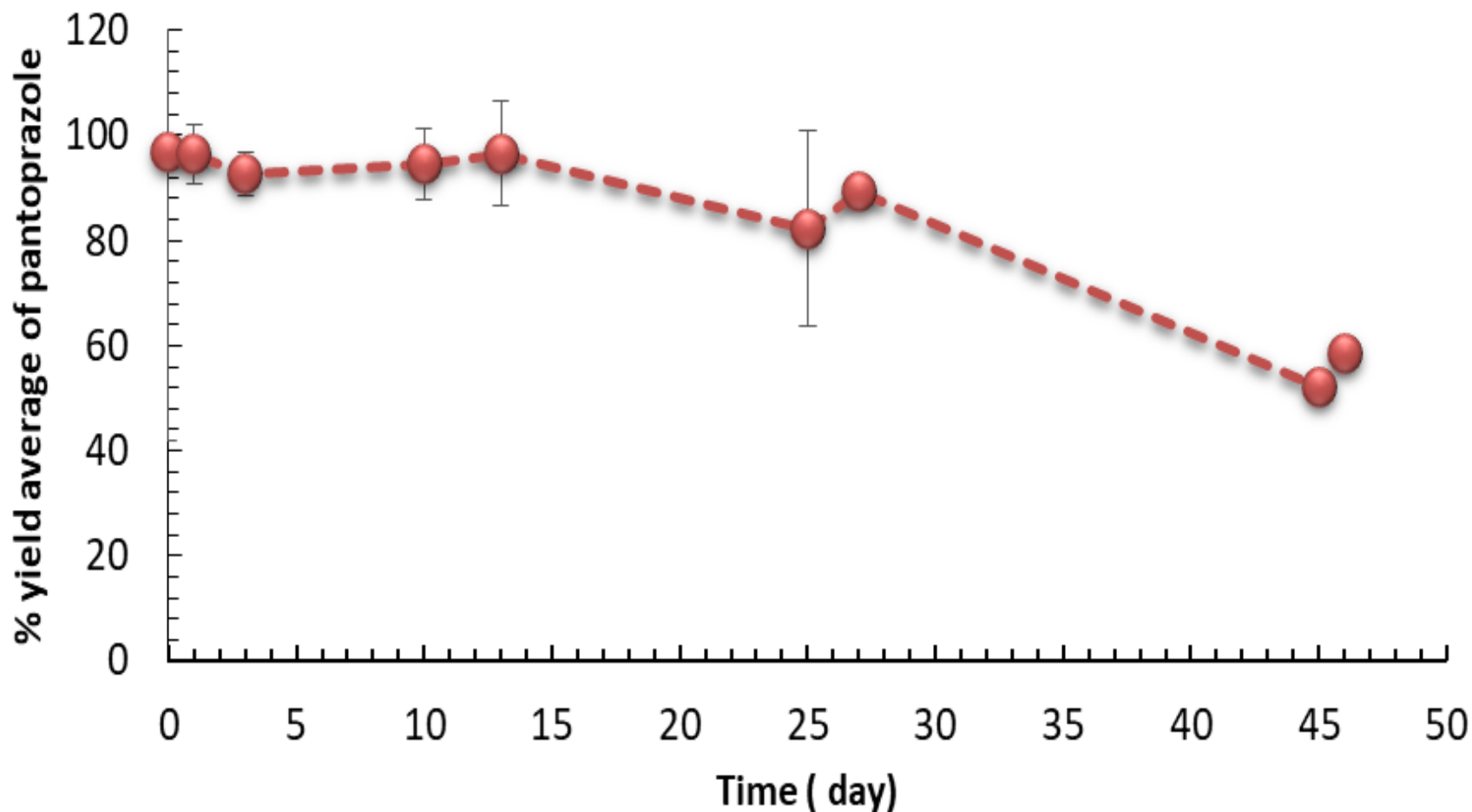
Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in water and preserved for the duration of the study at R.T

Pantoprazole suspension in water at 4°C:



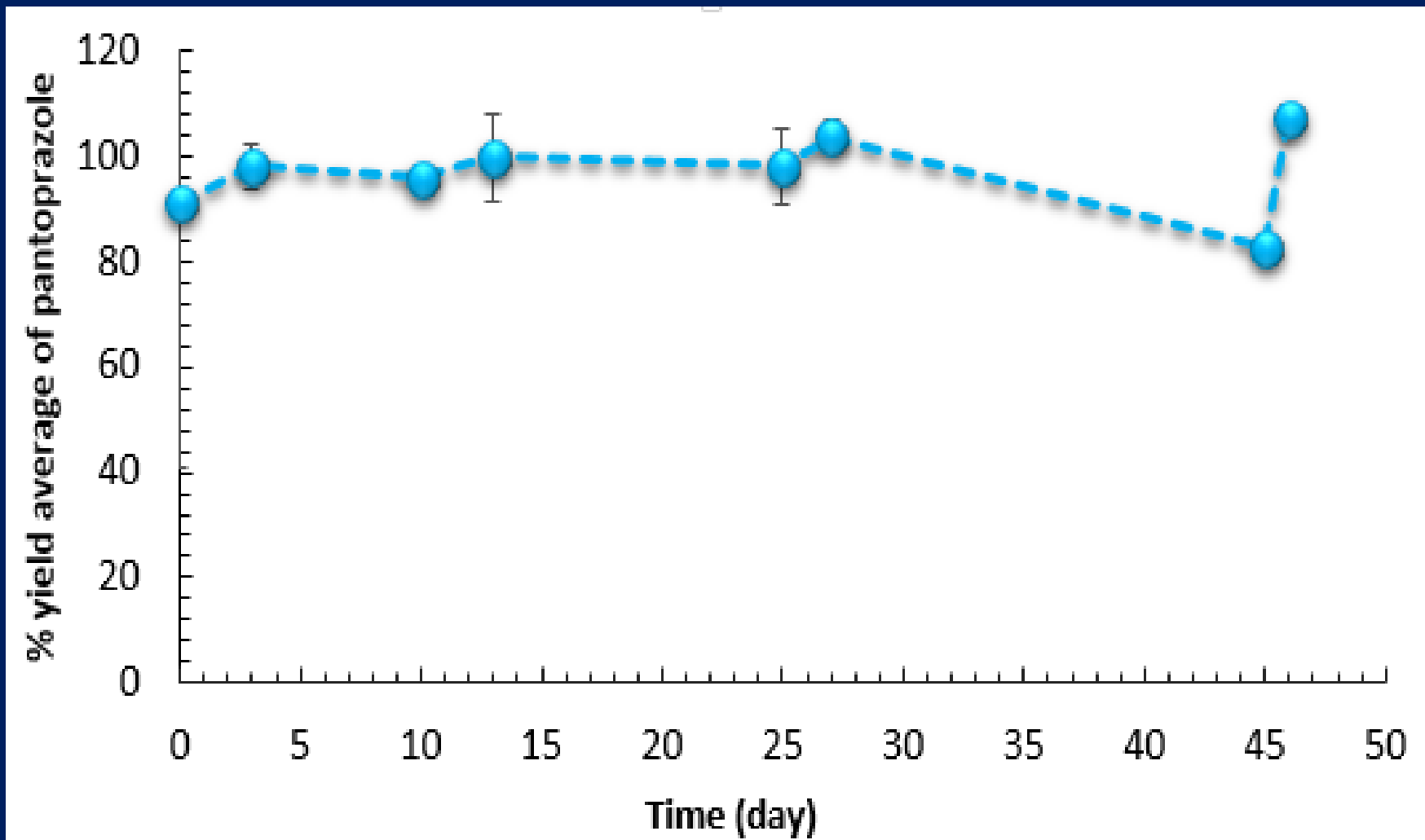
Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in water and preserved for the duration of the study at 4°C

Pantoprazole suspension in syrup at RT:



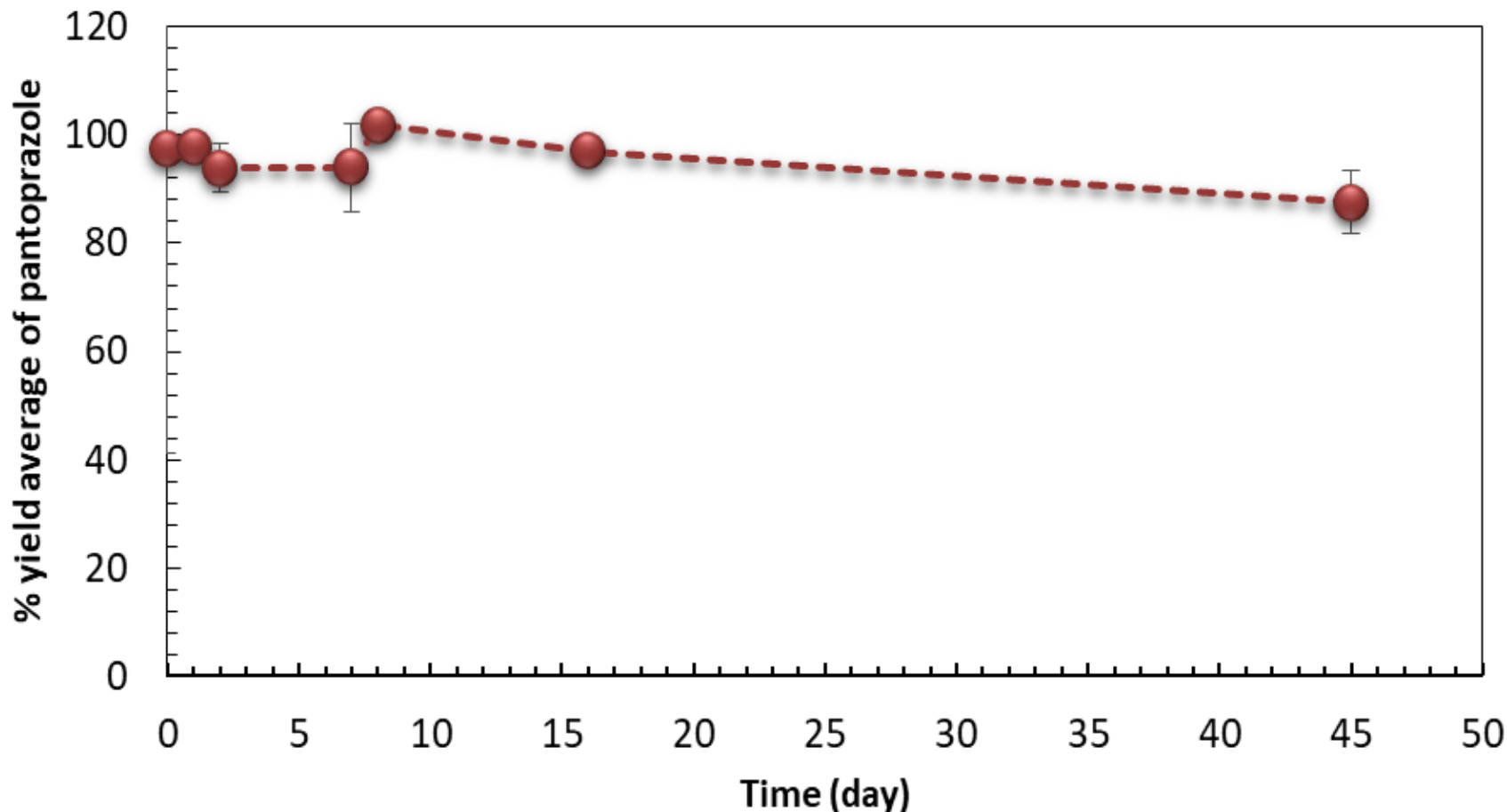
Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in syrup and preserved for the duration of the study at R.T

Pantoprazole suspension in syrup at 4°C.



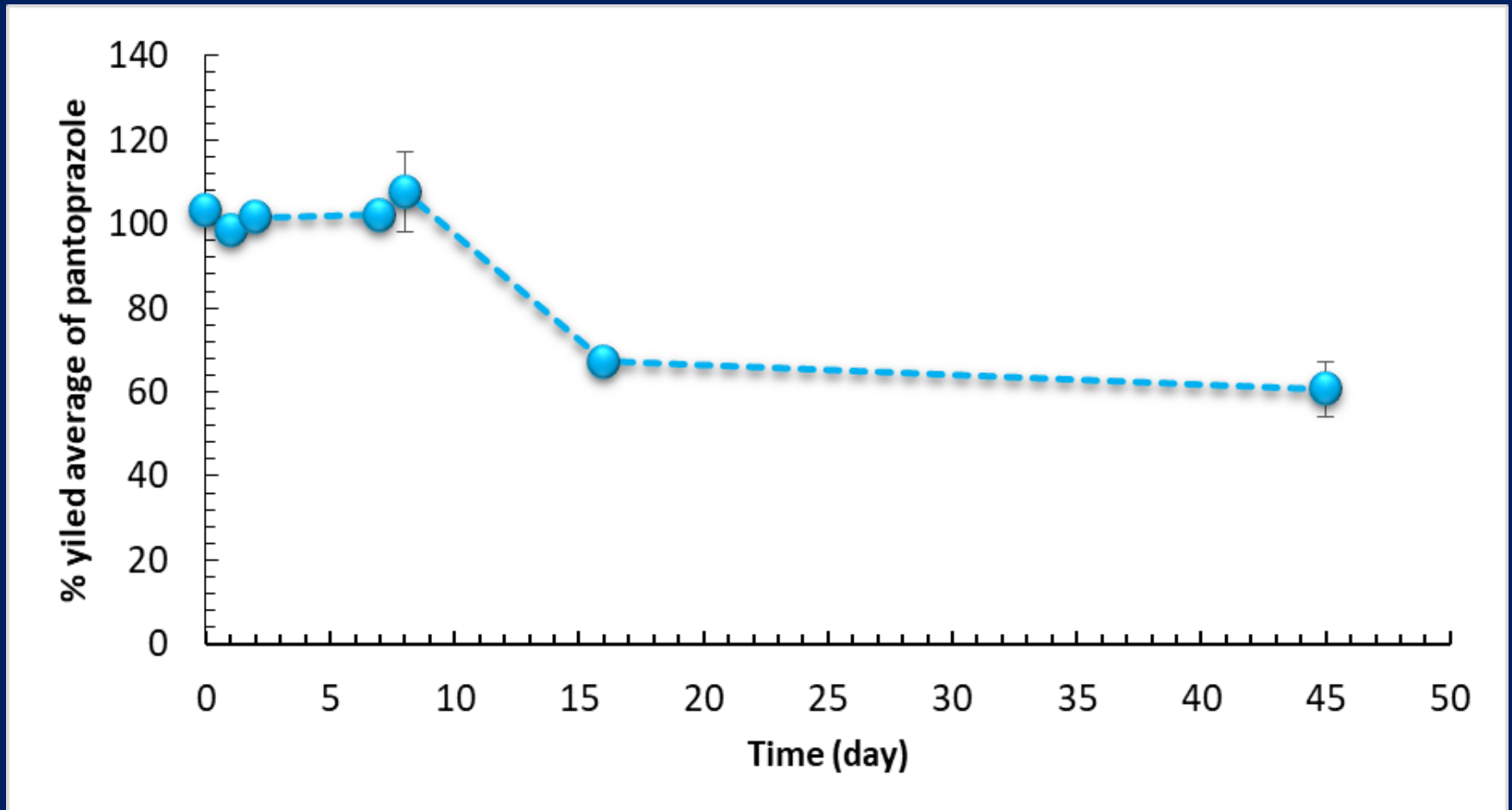
Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in syrup and preserved for the duration of the study at 4°C

Pantoprazole suspension in syrup using xanthan gum at R.T:



Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in xanthan gum suspension and preserved for the duration of the study at R.T.

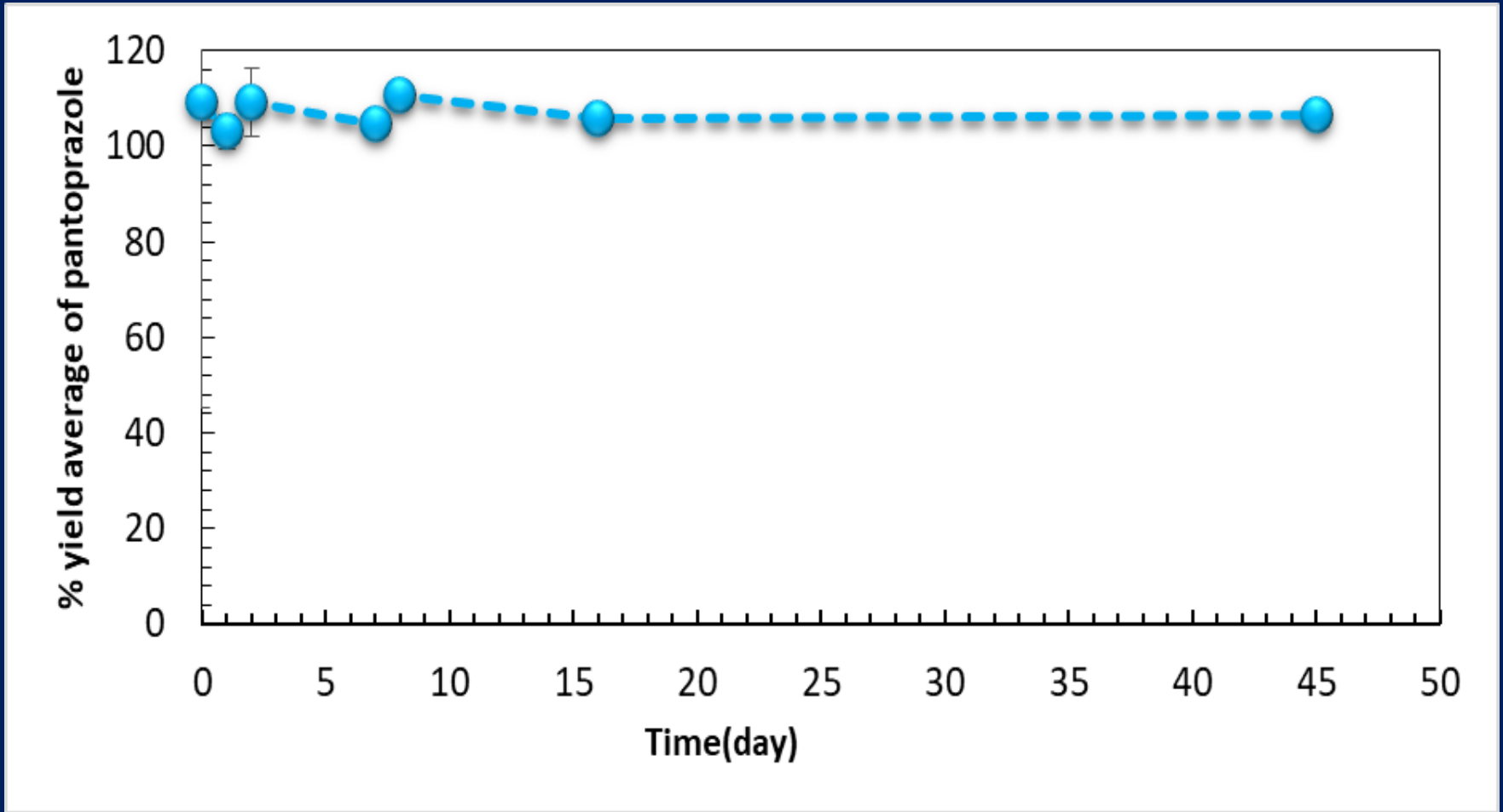
Pantoprazole suspension in syrup using xanthan gum 0.2 g/100ml at 4°C.



Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in xanthan gum suspension and preserved for the duration of the study at 4°C.

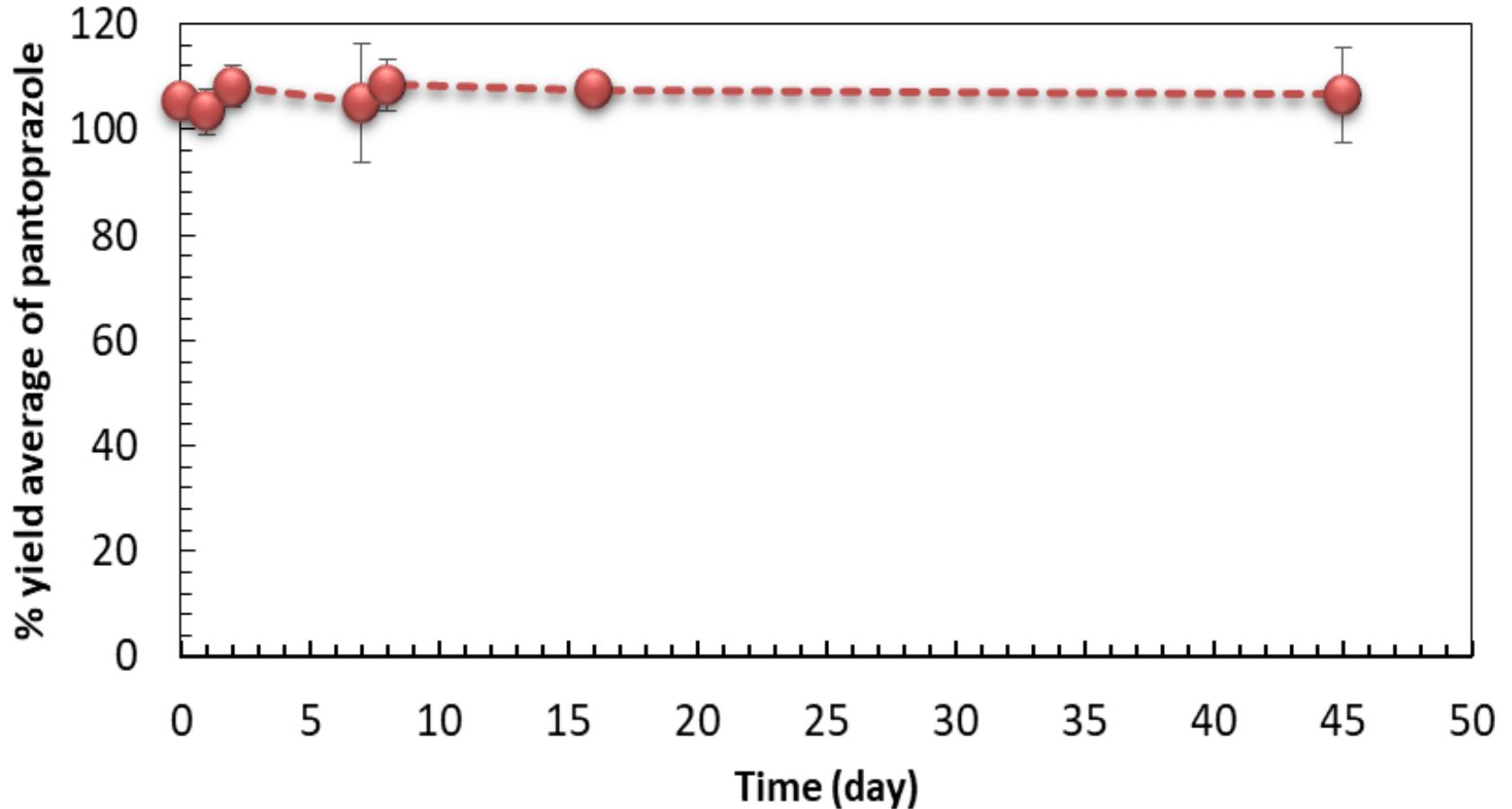
Pantoprazole suspension in syrup using CMC

0.2g/100ml at 4°C:



Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in CMC suspension and preserved for the duration of the study at 4°C.

Pantoprazole suspension in syrup using CMC 0.2g/100ml at R.T:

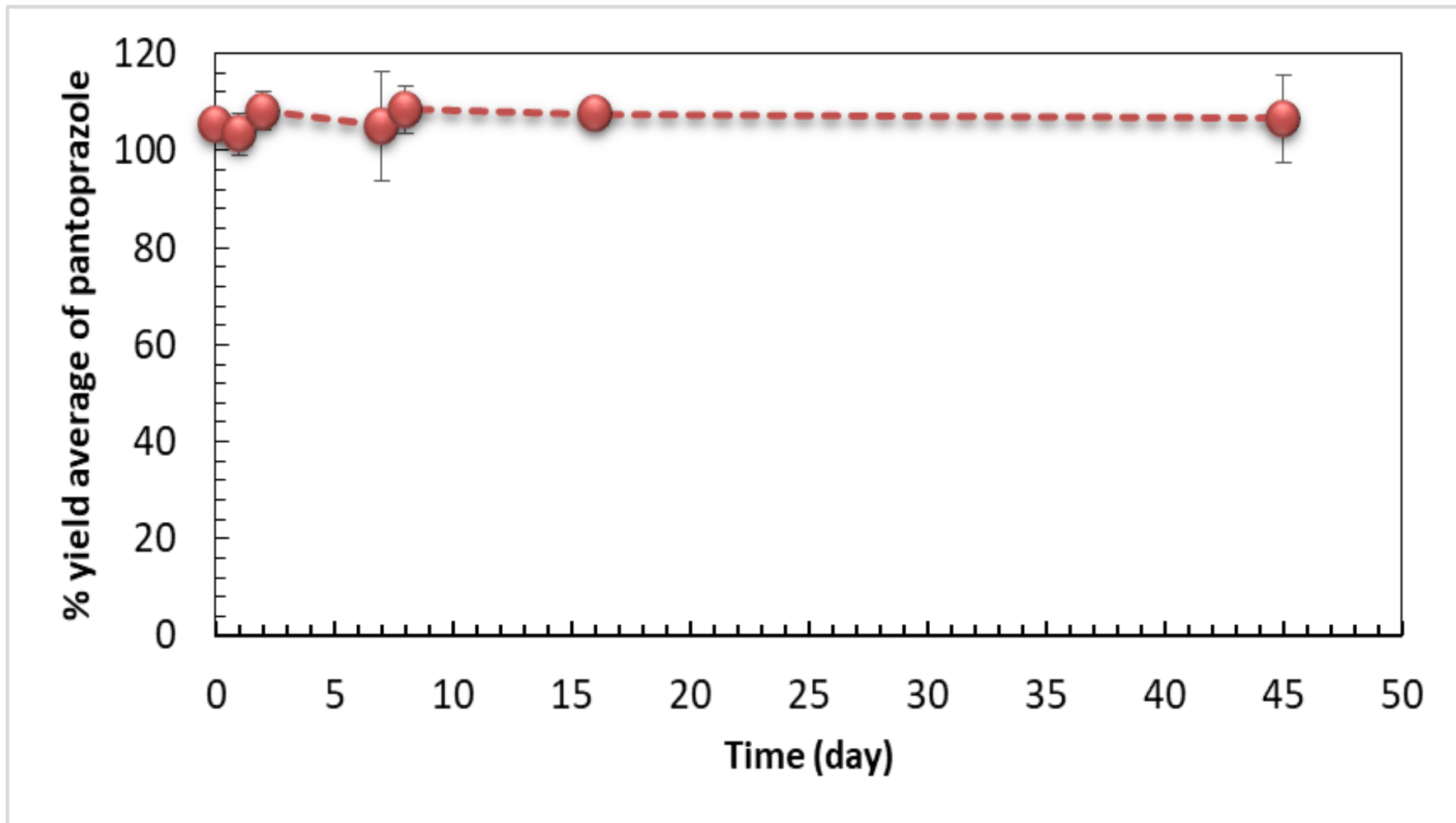


Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in CMC suspension and preserved for the duration of the study at R.T.

A summary of the “range” of the different preparations

Preparation	range
Pantoprazole in water at RT	8
Pantoprazole in water at 4C	22
Pantoprazole in syrup at RT	44
Pantoprazole in syrup at 4C	25.5
Pantoprazole Suspension with 0.2% xanthan gum at RT	14.5
Pantoprazole Suspension with 0.2% xanthan gum at 4C	13
Pantoprazole Suspension with 0.2% CMC at 4C	6
Pantoprazole Suspension with 0.2% CMC at RT	5

Best formula, Pantoprazole suspension in syrup using CMC 0.2g/100ml at R.T:



Percentage yield (actual/expected X100%) of samples taken from pantoprazole tablets dispersed in CMC suspension and preserved for the duration of the study at R.T.



- It is concluded that pre-formulation studies are vital prior to the compounding of extemporaneous preparations.
- These studies should include testing of the physico-chemical properties of the active ingredient, such as solubility, pka, and stability in aqueous solutions.



- oral liquids of Different drugs should not be prepared similarly.
- Not all suspending agents are equally suitable in stabilizing suspensions.



- Formulative considerations taken into account should include using suspending agents, viscosity modifying agents, and materials that prevent the hydrolysis or increase the stability of the active ingredient when applicable.
- Pharmacies that frequently prepare oral liquids must make use of helpful guidelines in this subject