Connecting Industry to Mathematics Instruction

NSF ATE Award # 1954291

Solutions: Subcutaneous Drug Delivery Implant Student Activity Sheet

A research associate at RTI helps to develop study designs, runs studies in the lab, collects data on a daily basis, runs all types of assays on the samples collected, analyzes data, and suggests changes to the study designs based on the data that is collected.

One thing that is being developed is an implant to disperse medication over a period of time to reduce the number of doctor visits needed, specifically for women in developing countries.

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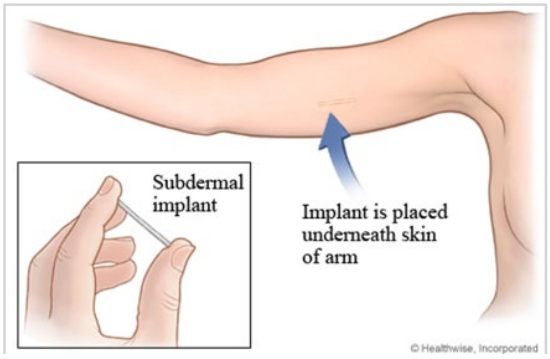
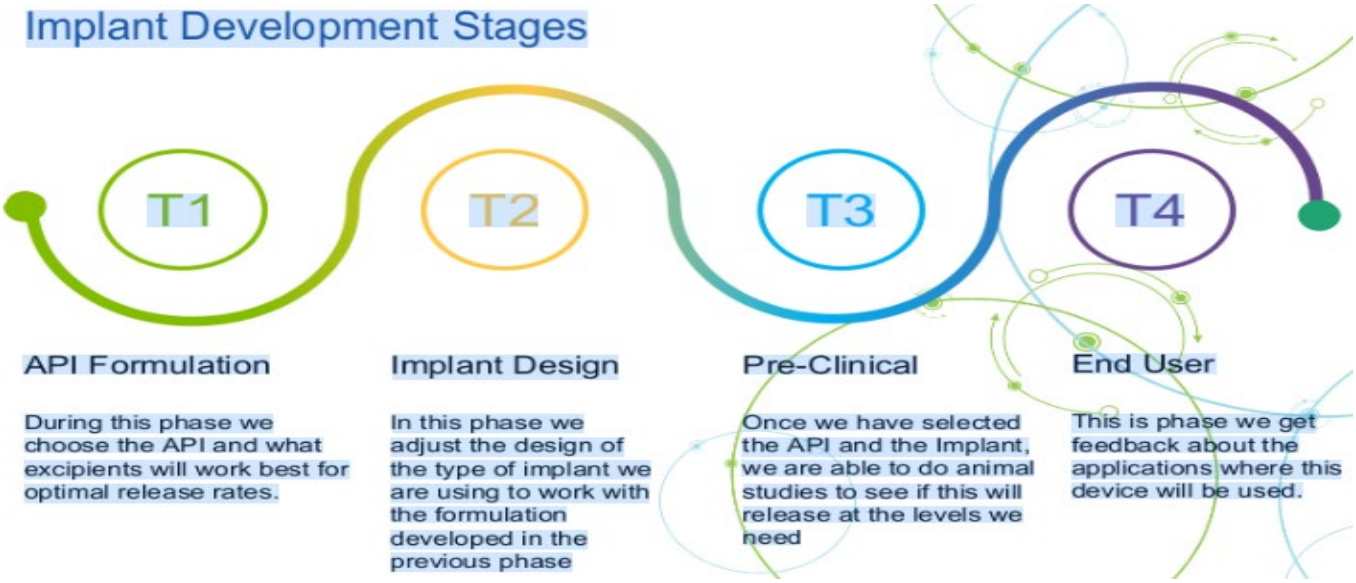


As a research associate for RTI, your job is to determine which Excipient (an inactive substance that serves as the vehicle or medium for a drug or other active substance) is best suited to use for the specific Active Pharmaceutical Ingredients (API). We need to see how much each combination releases on a daily basis. We will test this for 30 days. In order to be effective, the API “x” must stay above a minimum release rate of 20 ug/day and stay below the maximum release rate of 40 ug/day.



We will be focusing on T1 and T2.

T1 – API Formulation: As a research associate, your next steps will be to design a study, implement the study, collect data, and analyze/interpret the data.

DESIGN A STUDY

1. If you were designing this experiment, what are three elements you would include in your design? Please elaborate on your reasoning for your inclusions. (randomness, large enough sample, questions is clear)

IMPLEMENT STUDY

We will need to combine API "x" with the excipients available for subcutaneous (situate or applied under the skin) drug delivery in 4 excipients. We need to see how much each combination releases on a daily basis for a period of 30 days.

Remember, we want to reach a minimum release rate of 20 ug/day and maximum release rate of 40 ug/day for it to be effective.

For 30 days, we will place the combinations in an In vitro Study (occurs in a controlled environment) which will allow us to mimic the human conditions in which this drug/excipient combination will be exposed.

We will be collecting the sample daily (3 samples/3 times a day) to see how much drug has been released into the solutions to determine what is acceptable for this particular API.

2. What does RTI do in order to ensure that they have enough data to work with to give them the most accurate results? (they run triplicates of each combination)

DATA ANALYSIS

Using the data collected for the 4 different Excipients by RTI's Lab Technician provided in the EXCEL worksheet (HERE), compute the following and record in the spreadsheet. For questions 3 and 4, include your results on your spreadsheet.

3. For each excipient:
    a. Calculate the mean
    b. Calculate the standard deviation
    c. What do the mean and standard deviation tell you about the APIs?(the average of the ugs that is being dispersed for each excipient and the distance away from the mean – a higher standard deviation would not be beneficial to the study)

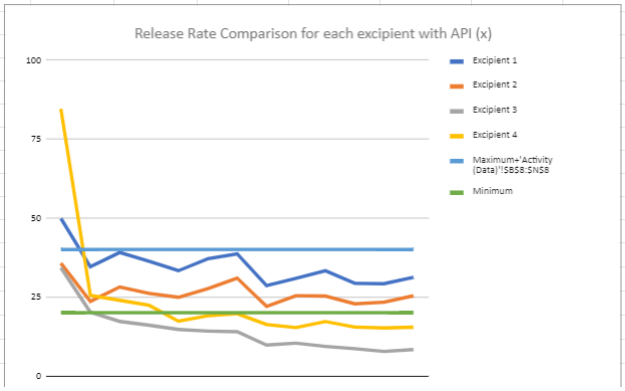
4. Graph the daily release points on a line graph. Include:
    a. Low acceptable release drug limit
    b. High acceptable release drug limit
    c. What type of graph is most useful? Why? (the line graph because you can show the min and max and easily see which excipient falls between)

5. Describe the data for each excipient (SOCS).(Excipient #4 has the most spread which may be caused by the outlier. Excipient #1-3 have closer spreads and don't appear to have an outlier. Excipient #1 has a mean on the high end, but levels off and remains in the range after the initial release and may be worth looking into further. Excipient #2 is the best option for staying in the required range and should move on to the next stage.)

6. What trends do you see in the data?(All of the excipients start off with a high release, but then level off. Excipient #1 and 2 stay in the required range. Excipient #3 and 4 go too low after the initial high release)

7. Given the data, which excipient best fits in-between the acceptable drug release limits for the API? Explain your reasoning.

	1	4	6	8	11	13	15	18	20	22	25	29	32	mean	deviation
Excipient #1	49.79598431	34.57446765	39.04826967	36.27951357	33.3062702	37.09003742	38.62304111	28.54377397	30.89175793	33.29808418	29.27617931	29.15824385	31.15845499	34.69569832	5.769100256
Excipient #2	35.64293709	23.56456774	28.09278942	26.11840685	24.85878691	27.60872521	30.95498902	21.988949	25.39598305	25.27255735	22.80704027	23.30569129	25.3478143	26.22763365	3.718671233
Excipient #3	34.25756056	20.17845406	17.23910922	16.04263171	14.67700233	14.18071567	13.96741083	9.776387772	10.345152	9.301796473	8.589614772	7.736600341	8.338724217	14.20239692	7.170472779
Excipient #4	84.5333303	25.46113395	23.92498345	22.3346584	17.32866119	19.0337334	19.6794408	16.23828497	15.2777682	17.17306814	15.44506017	15.14748008	15.41498988	23.61481484	18.62635241
Min Release	40	40	40	40	40	40	40	40	40	40	40	40	40		
Max Releas	20	20	20	20	20	20	20	20	20	20	20	20	20		



8. Does the standard deviation ever help you eliminate an excipient? Explain.(we can eliminate Excipient #4 – if falls a little below the minimum, but more importantly, the standard deviation is so high which means that the data is more spread out and is less reliable that we would not want to use it in our next part of our study)

INTERPRET THE DATA

9. What do you think are other variables that may play a part in the effectiveness of the implant? (see teacher notes)

10. What recommendation(s) would you make to RTI based on the results you've gathered? (which excipients need more testing?) Explain your reasoning. (Excipient #1 and 2 should be investigated further - they fall in the parameters (or close to it). #3 and 4 can be eliminated at this stage - they fall too far out and the standard deviation is too high)

T2 – Implant Design: As a research associate, your next step will be to adjust the design of the implant. We will adjust the polymer (natural or synthetic material) and the diameter of the device.

We want to know which polymer and diameter size will work with the combination of drug/excipient from the T1. (API's Acceptable Drug release limits must be in-between 20ug/day and 40ug/day.)

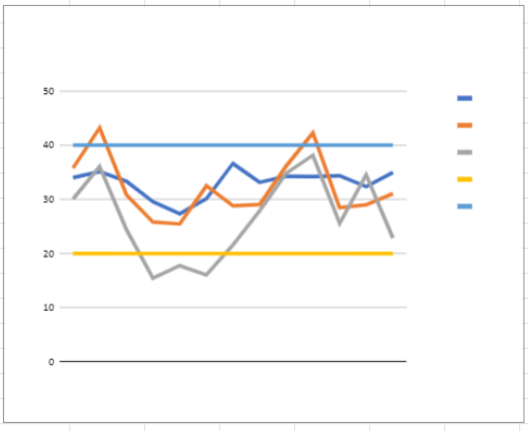
How would you design an experiment to determine which polymer and diameter size would be best to use if we have 3 different polymers and 3 different sizes that are recommended to consider? (see below)

1. For each excipient and diameter size:
    a. Calculate the mean
    b. Calculate the standard deviation

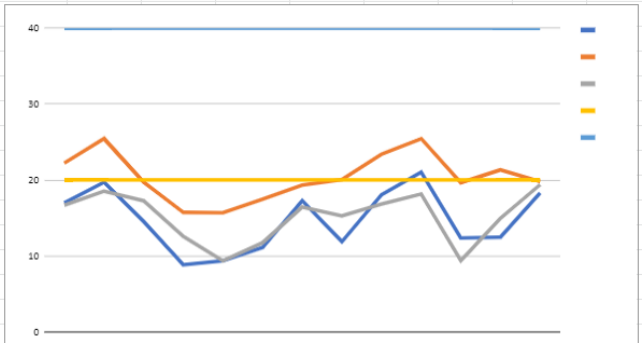
2. Graph the daily release points on a line graph: Include:
    a. Low acceptable release drug limit
    b. High acceptable release drug limit

3. What do you conclude from the data? Explain. (Polymer B could be eliminated. Polymer A size 50mm can be studied further and Polymer C size 100mm stays in the boundaries the best, but 50mm and 200mm are very close and could be studied further.)

Polymer A	1	4	6	8	11	13	15	18	20	22	25	29	32	mean	standard devi
50 mm	33.99701	35.10529	33.33398	29.57207	27.34095	30.11945	36.60591	33.13502	34.24093	34.20976	34.36256	32.34764	34.95749	33.02523	2.577803
100 mm	35.78720	43.19703	30.83000	25.80360	25.46974	32.48952	28.80896	29.04067	36.14235	42.28689	28.46503	29.00375	31.05836	32.18331	5.673089
200 mm	30.04578	36.07240	24.45802	15.47077	17.78214	16.05218	21.59305	27.88166	34.83305	38.13841	25.59864	34.52722	22.88017	26.56411	7.769346
min	20	20	20	20	20	20	20	20	20	20	20	20	20		
max	40	40	40	40	40	40	40	40	40	40	40	40	40		



Polymer B	1	4	6	8	11	13	15	18	20	22	25	29	32		
50 mm	16.97137	19.68883	14.50900	8.819764	9.338586	11.09120	17.26051	11.87328	18.02920	21.02686	12.34193	12.45386	18.29652	14.74622	4.037343
100 mm	22.22111	25.45482	19.69377	15.72270	15.66809	17.46885	19.32167	20.04109	23.38817	25.43400	19.62883	21.33717	19.78214	20.39711	3.157566
200 mm	16.65908	18.51564	17.24974	12.55274	9.330889	11.70287	16.41868	15.26886	16.83032	18.13031	9.366820	14.93840	19.37859	15.10330	3.356291
min	20	20	20	20	20	20	20	20	20	20	20	20	20		
max	40	40	40	40	40	40	40	40	40	40	40	40	40		



Polymer C	1	4	6	8	11	13	15	18	20	22	25	29	32		
50 mm	26.50981	33.49999	39.53482	23.89290	19.95685	20.43145	33.39362	29.40304	27.91913	33.97930	18.20448	24.32805	34.07868	28.08709	6.566782
100 mm	39.53355	39.39114	31.72717	23.28243	26.53048	28.57996	35.03474	33.74018	30.64000	36.51073	20.39053	28.07727	37.69521	31.62565	6.084689
200 mm	33.49953	31.90562	29.02337	17.11729	23.84207	28.43956	16.50276	25.21069	32.40759	32.25744	18.51077	26.63009	34.31623	26.89716	6.298053
min	20	20	20	20	20	20	20	20	20	20	20	20	20		
max	40	40	40	40	40	40	40	40	40	40	40	40	40