PK Simulations of 100 mg Oral Medication in Patients with Modified CL and F

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December 7, 2015

```
# required libraries
library("PKPDmisc")
library("ggplot2")
library("dplyr")
```

```
##
## Attaching package: 'dplyr'
##
## The following objects are masked from 'package:stats':
##
##     filter, lag
##
## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

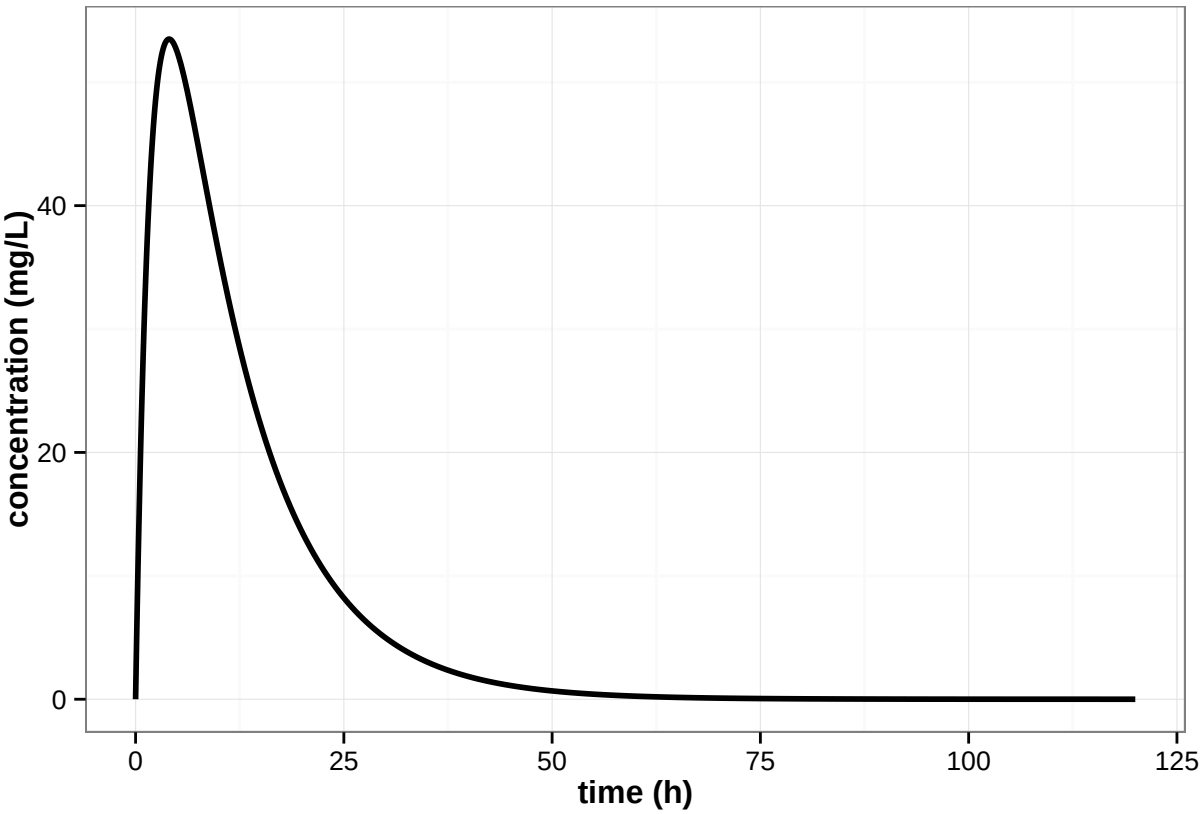
```
library("mlxR")
library("reshape2")
library("knitr")
```

```
knitr::opts_chunk$set(echo=FALSE)
```

ORAL FORMULATION

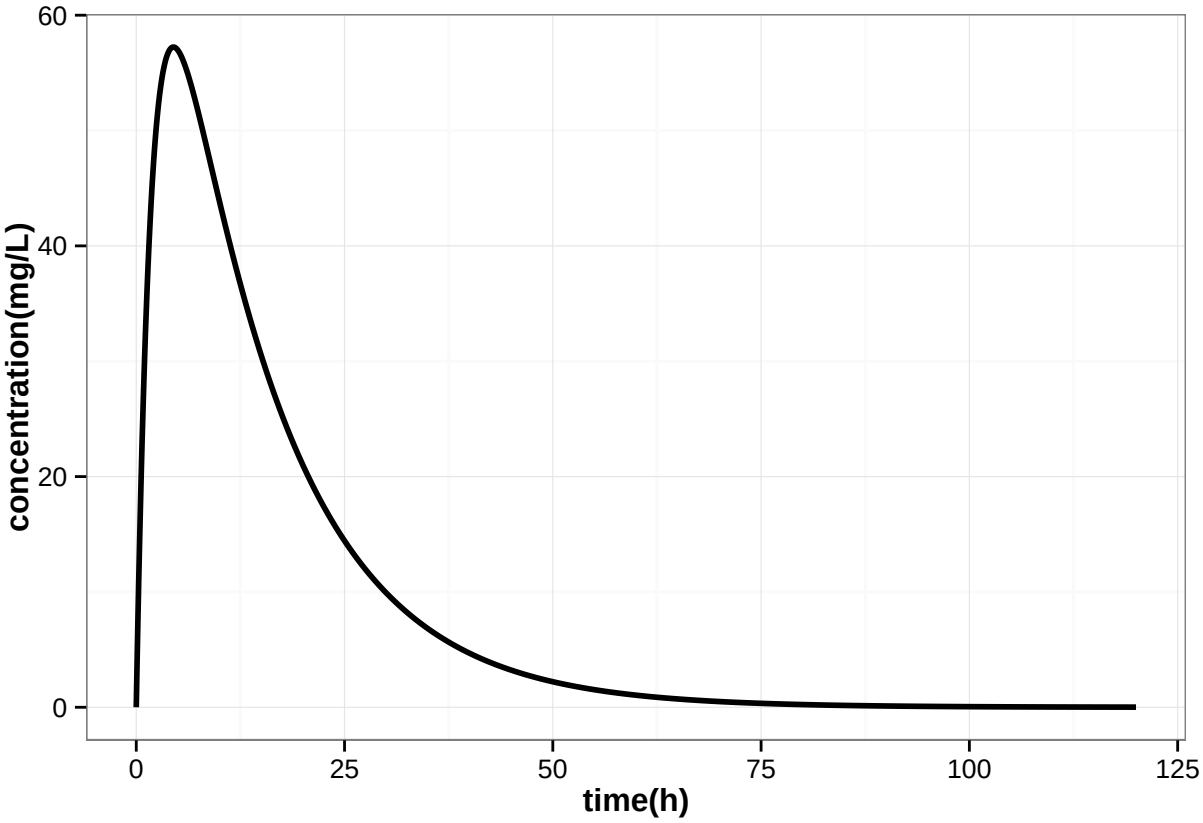
1. PK profile of 100 mg oral (SD)

(PK profile of 100 mg oral, SD (t=0), CL = 0.1 L/hr, V = 1 L, ka = 0.5/hr, F = 0.8)



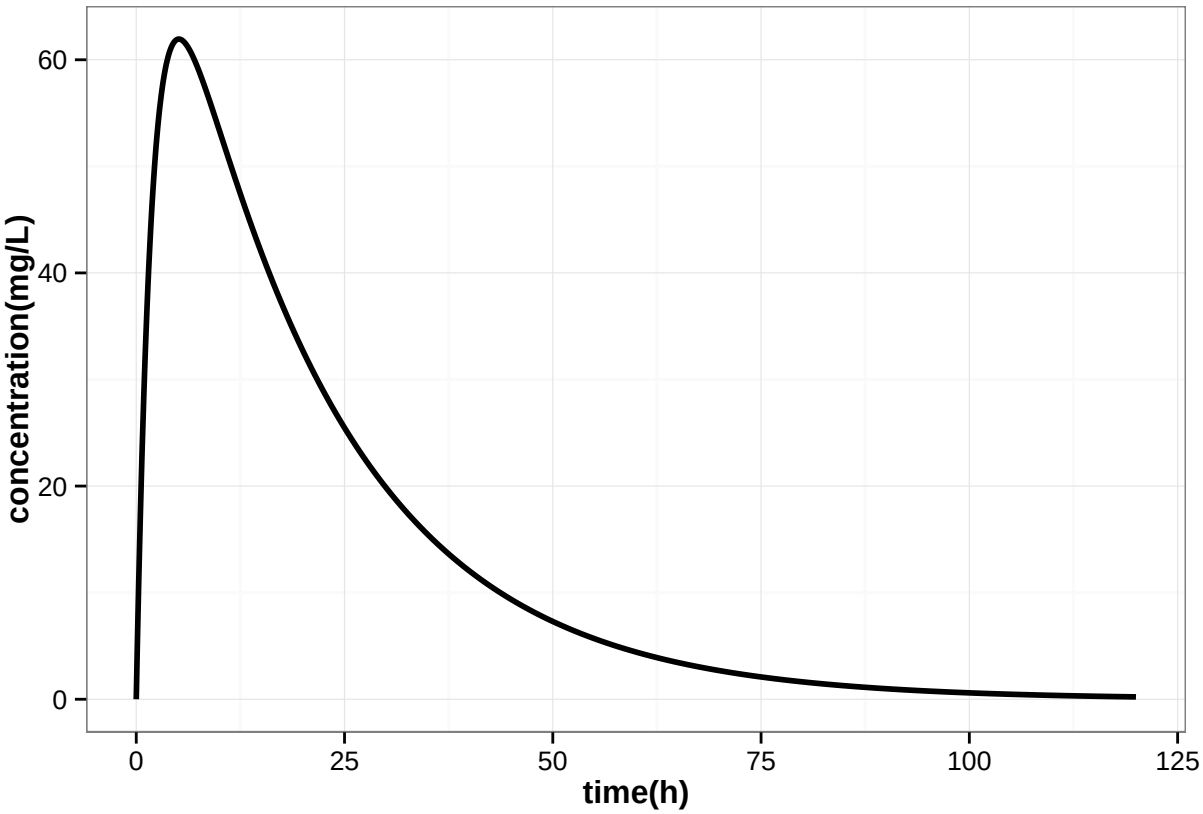
1a. Patient's clearance decreases by 25%.

(PK profile of 100 mg oral, SD (t=0), CL = 0.075 L/hr, V= 1 L, ka = 0.5/hr, F=0.8)



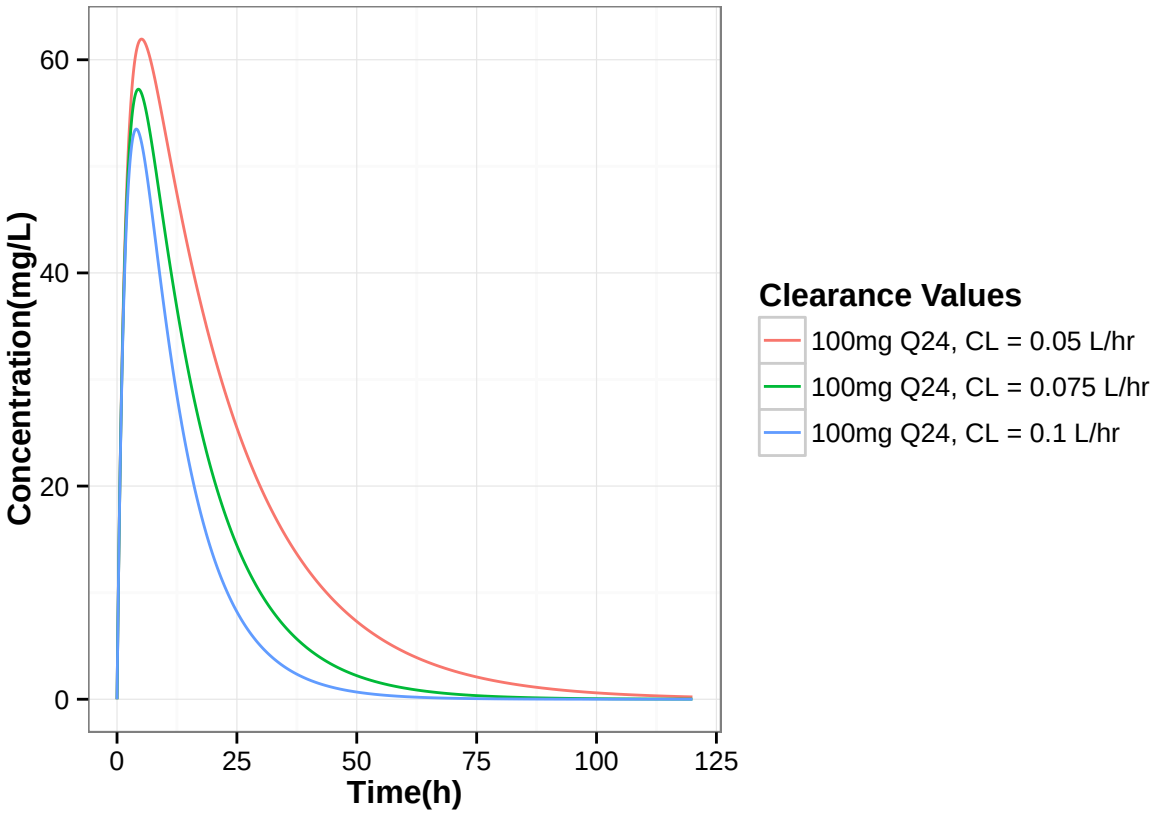
1b. Patient's clearance decreases by 50%.

(PK profile of 100 mg oral, SD (t=0), CL = 0.05 L/hr, V= 1 L, ka = 0.5/hr, F =0.8)



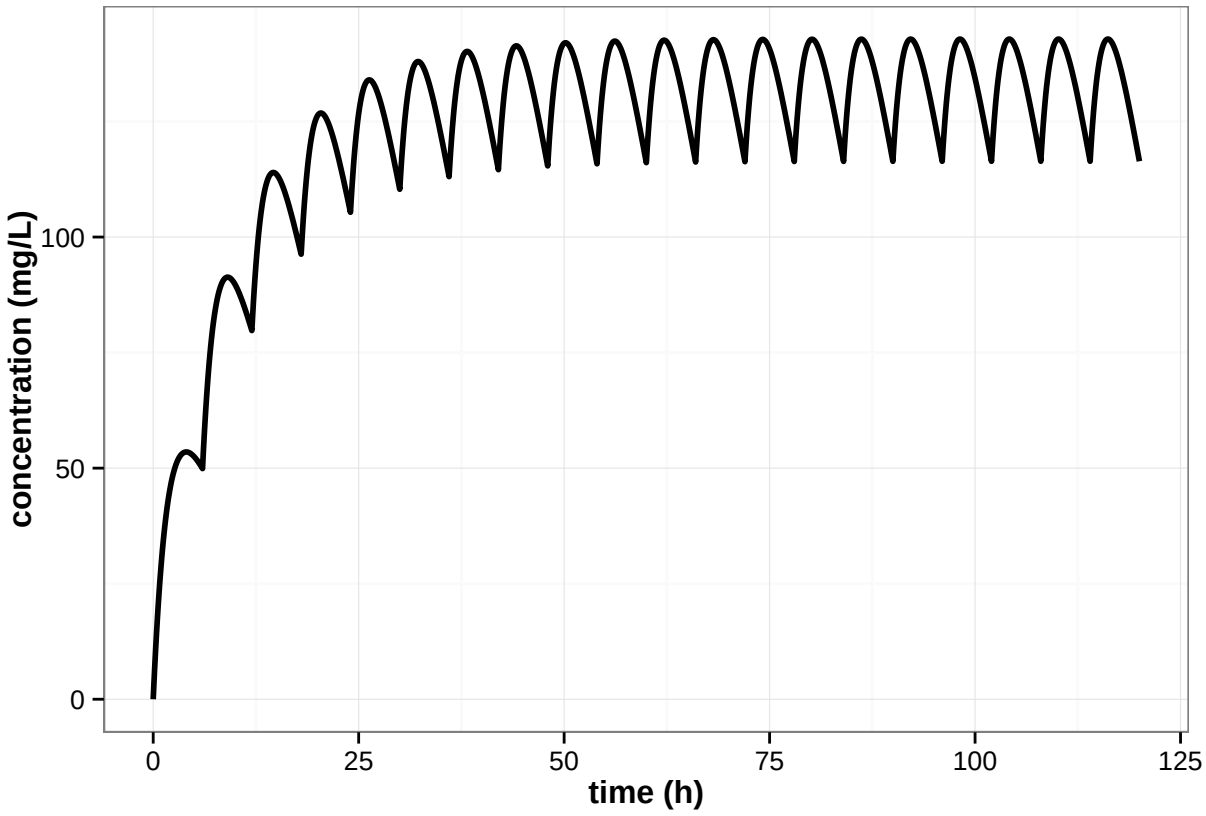
1c. Overlay plot of patient with decreased clearance and normal clearance.

(PK profile of 100 mg oral, SD (t=0), CL = 0.1, 0.075, 0.05 L/hr, V=1, ka = 0.5/hr, F = 0.8)



2. Patient is administered 100 mg oral loading dose and a 100 mg maintenance dose every 6 hours.

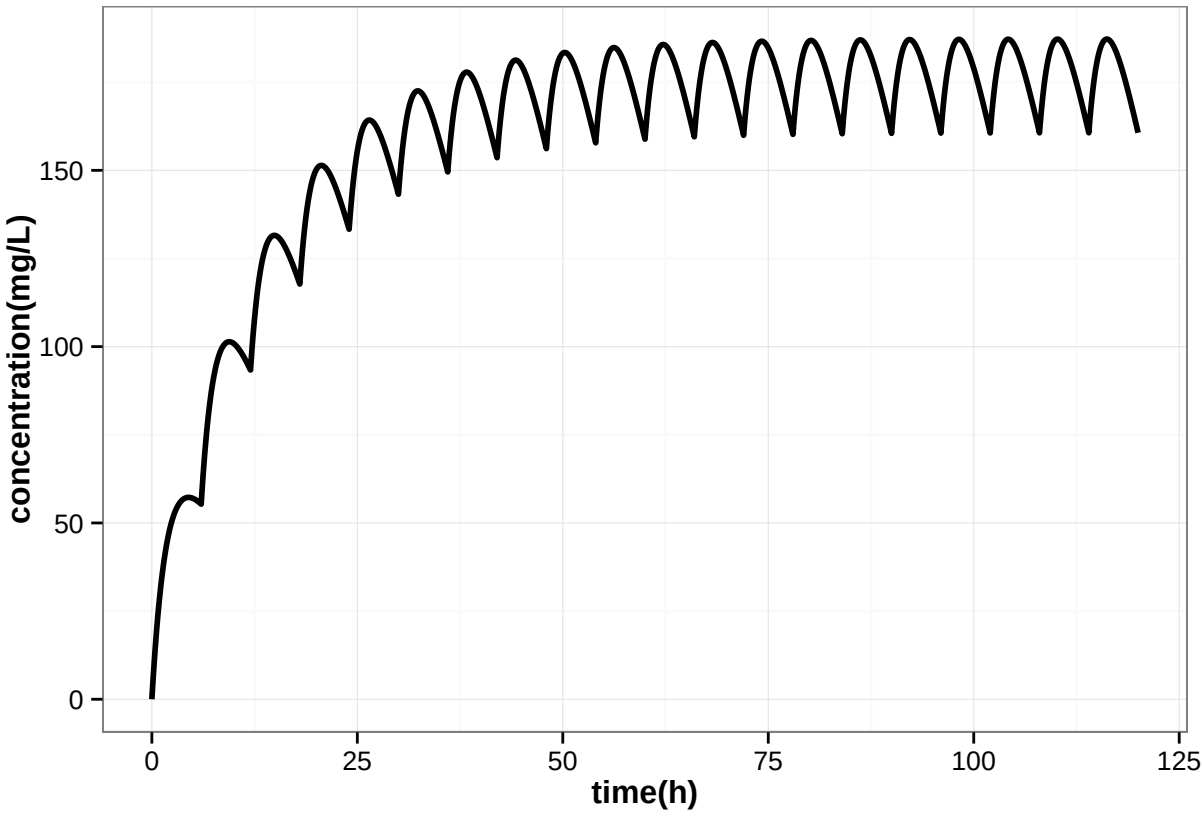
(PK profile of 100 mg oral, LD (t=0), MD (q= 6 hr), CL = 0.1 L/hr, V = 1 L, ka = 0.5/hr, F =



0.8)

2a. Patient's clearance decreases by 25%.

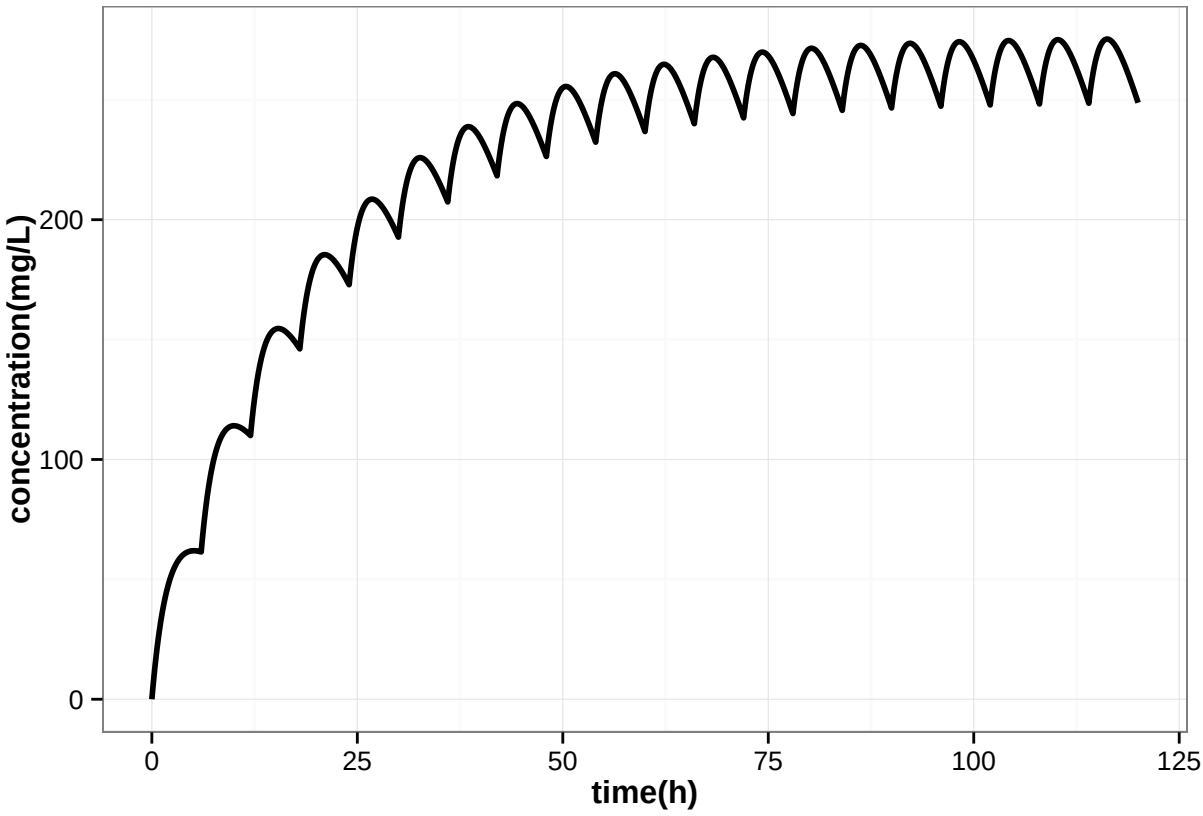
(PK profile of 100 mg oral, LD (t=0), MD (q= 6 hr), CL = 0.075 L/hr, V= 1 L, ka = 0.5/hr,



F=0.8)

2b. Patient's clearance decreases by 50%.

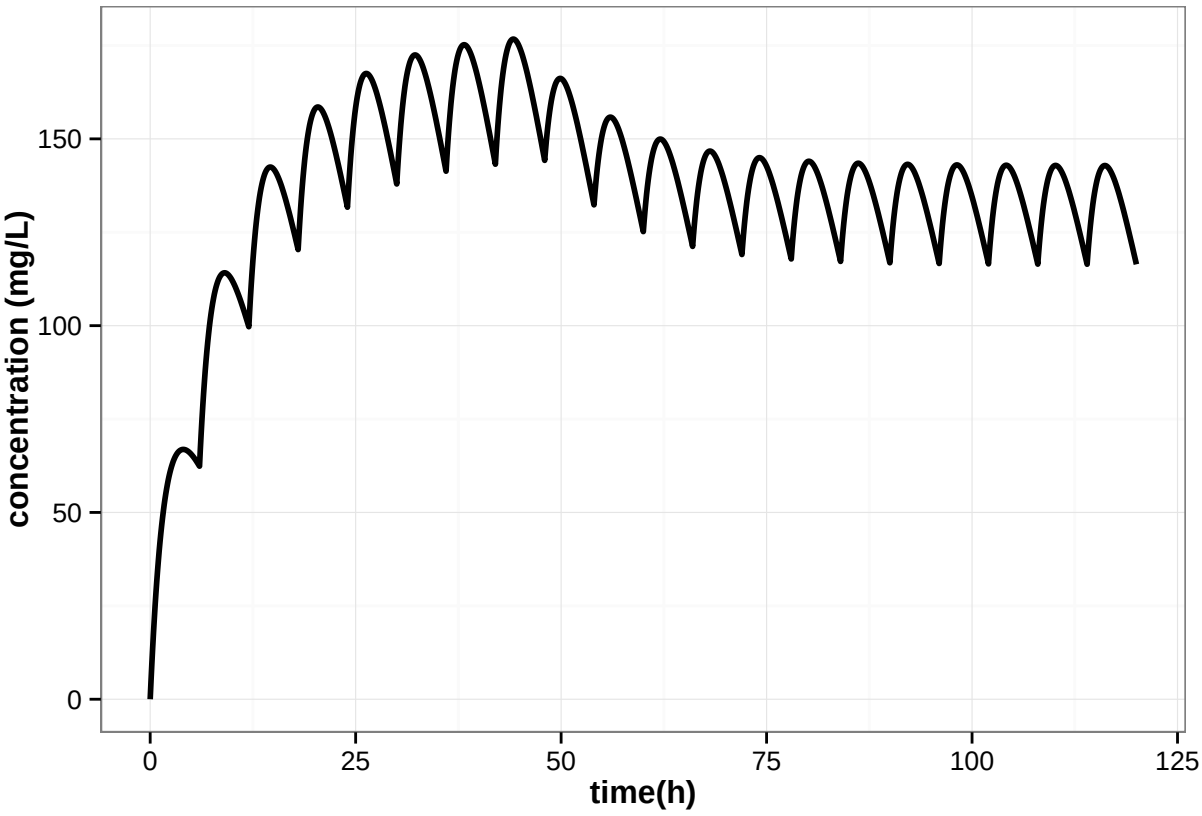
(PK profile of 100 mg oral, LD (t=0), MD (q= 6 hr), CL = 0.05 L/hr, V= 1 L, ka = 0.5/hr,



F=0.8)

2c. Patient consumes a high fat meal 48 hours after beginning treatment, which reduces bioavailability by 50%.

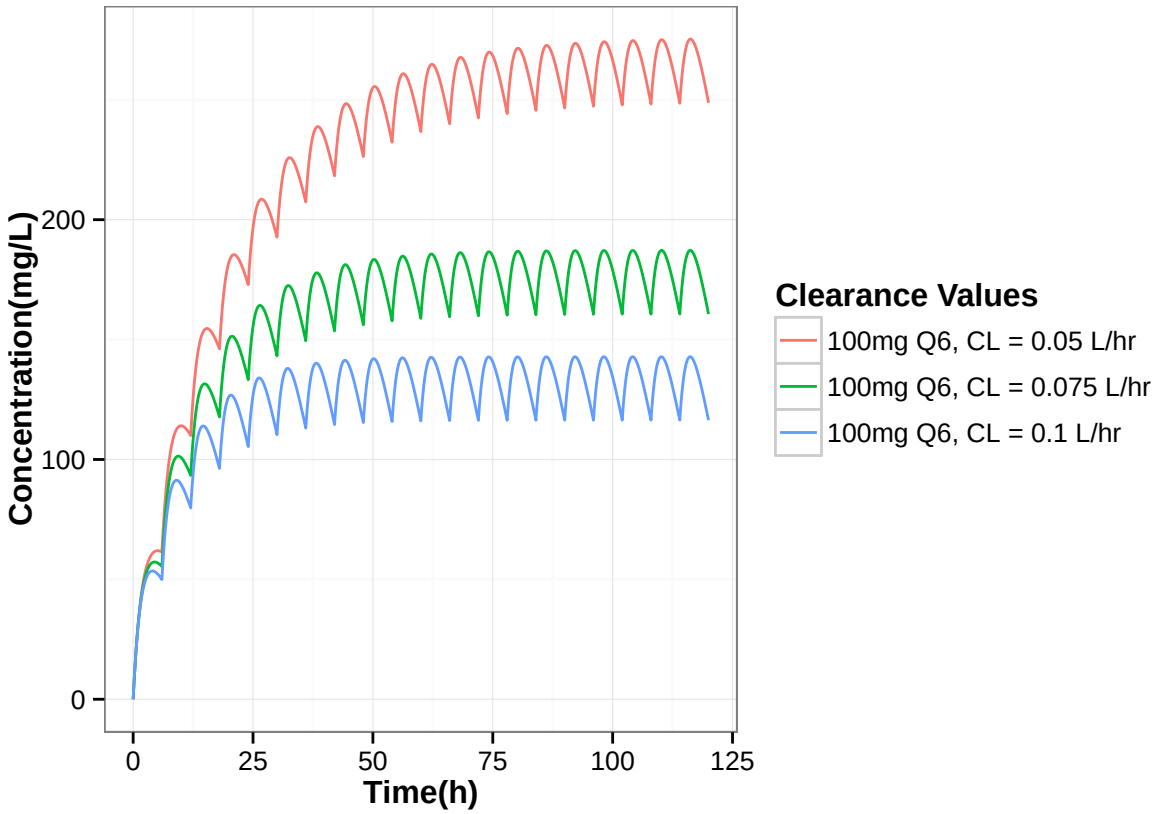
(PK profile of 100 mg oral, LD (t=0), MD (q=6 hr), CL = 0.1 L/hr, V = 1 L, ka = 0.5/hr,



F=0.8, 0.4)

2d. Overlay plot of patient with decreased clearance and normal clearance.

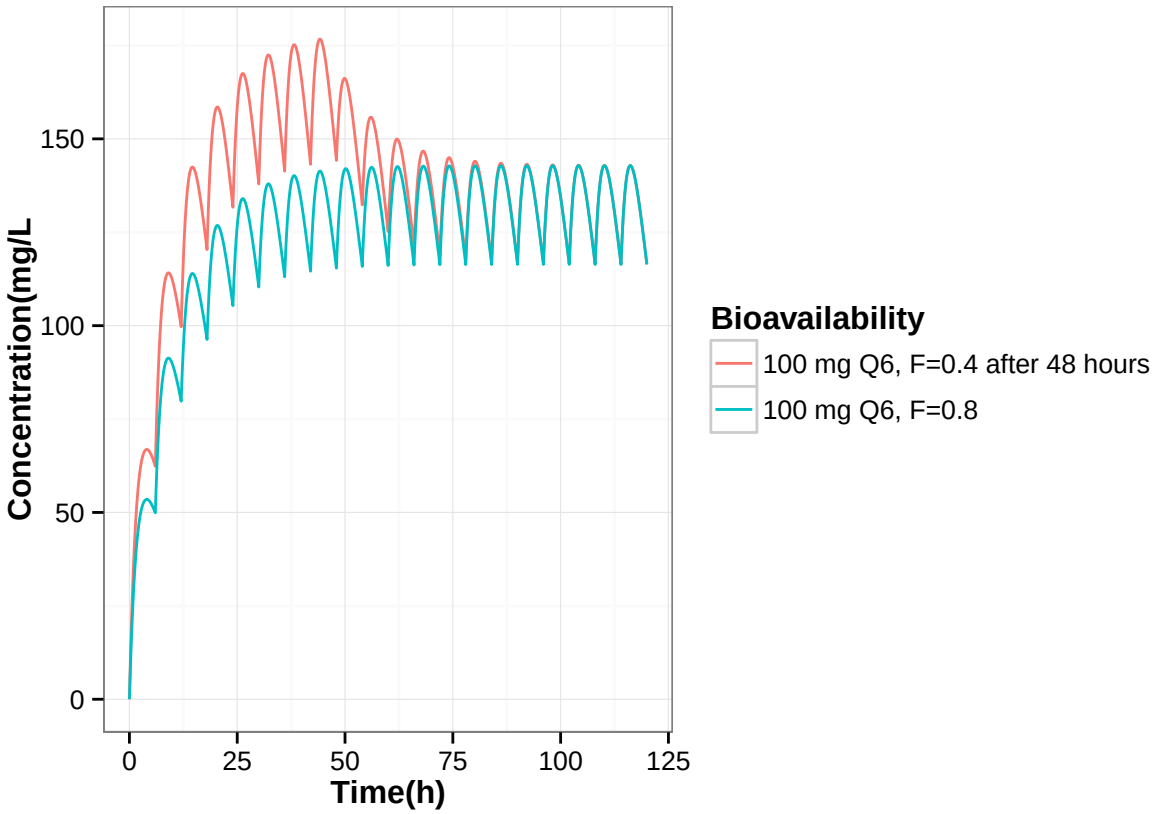
(PK profile of 100 mg oral, LD (t=0), MD (q=6 hr), CL = 0.1, 0.075, 0.05 L/hr, V = 1 L, ka =



0.5/hr, F=0.8)

2e. Overlay plot of patient with normal bioavailability and decreased bioavailability after consuming high fat meal.

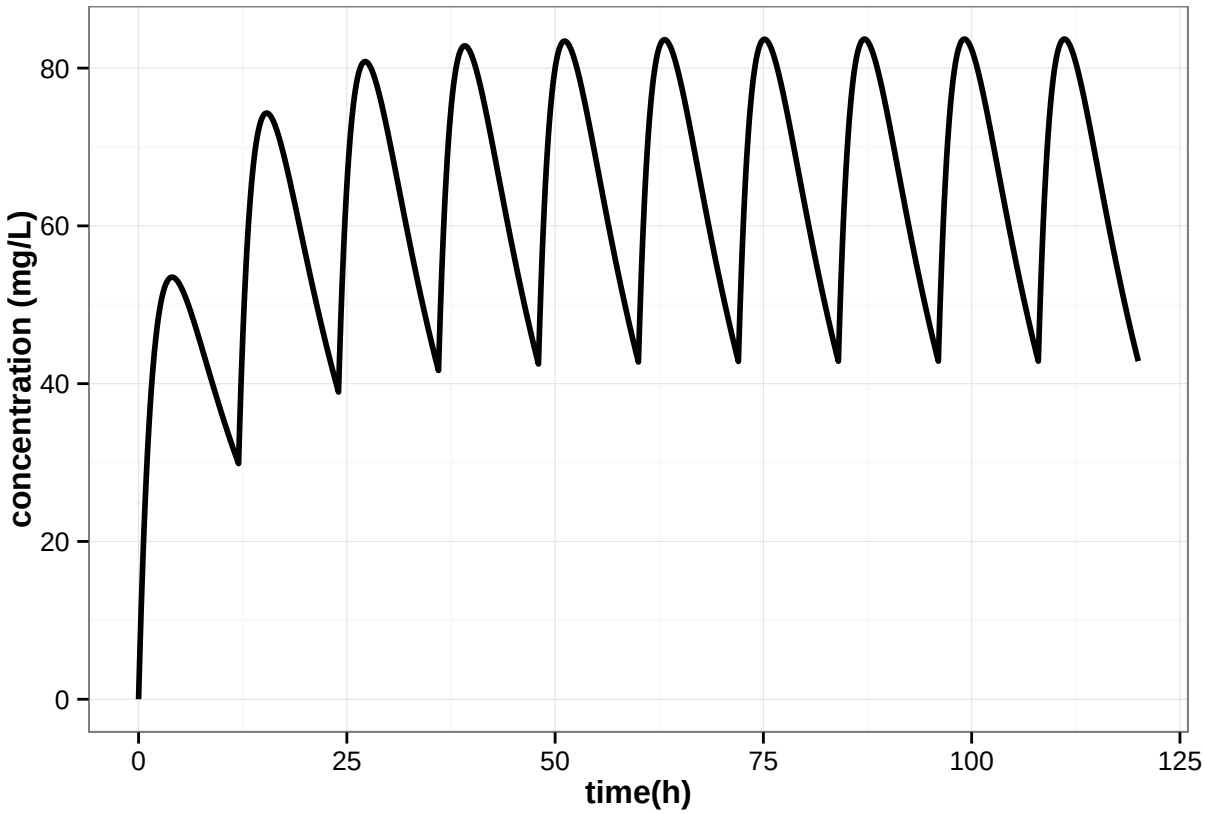
(PK profile of 100 mg oral, LD (t=0), MD (q=6 hr), CL = 0.1 L/hr, V = 1 L, ka = 0.5/hr,



F=0.8, 0.4)

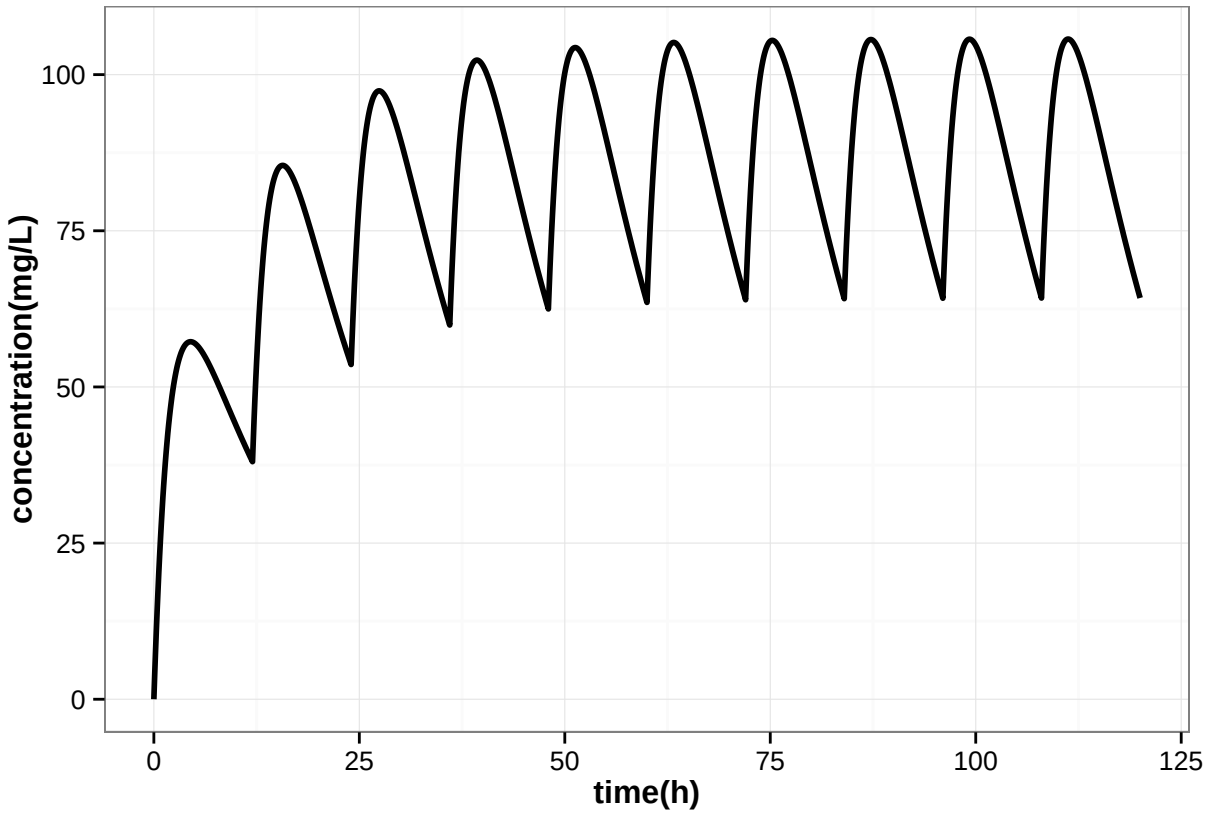
3. Patient is administered 100 mg oral loading dose, followed by a maintenance dose of 100 mg every 12 hours.

(PK profile of 100 mg oral, LD (t=0), MD (q=12 hr), CL=0.1 L/hr, V=1L, ka=0.5/hr, F=0.8)



3a. Patient's clearance decreases by 25%.

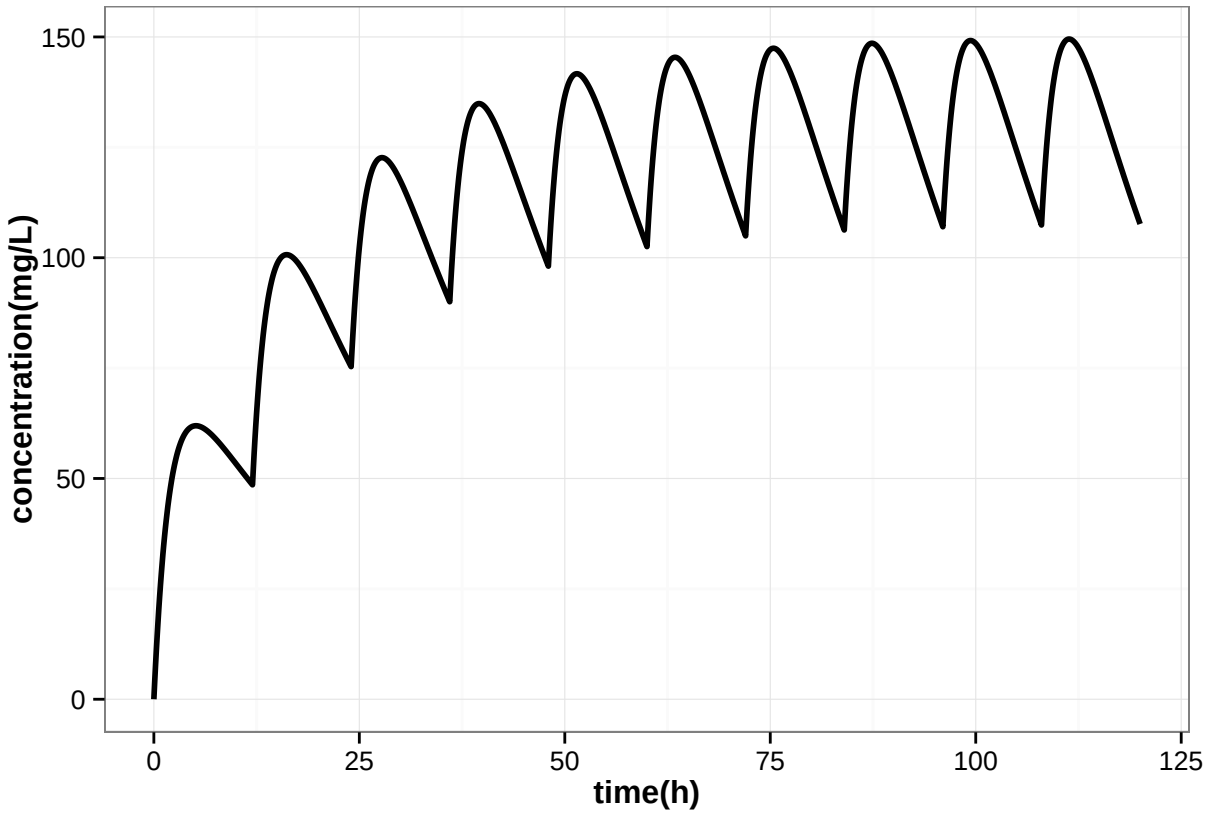
(PK profile of 100 mg oral, LD (t=0), MD (q= 12 hr), CL = 0.075 L/hr, V= 1 L, ka = 0.5/hr,



F=0.8)

3b. Patient's clearance decreases by 50%.

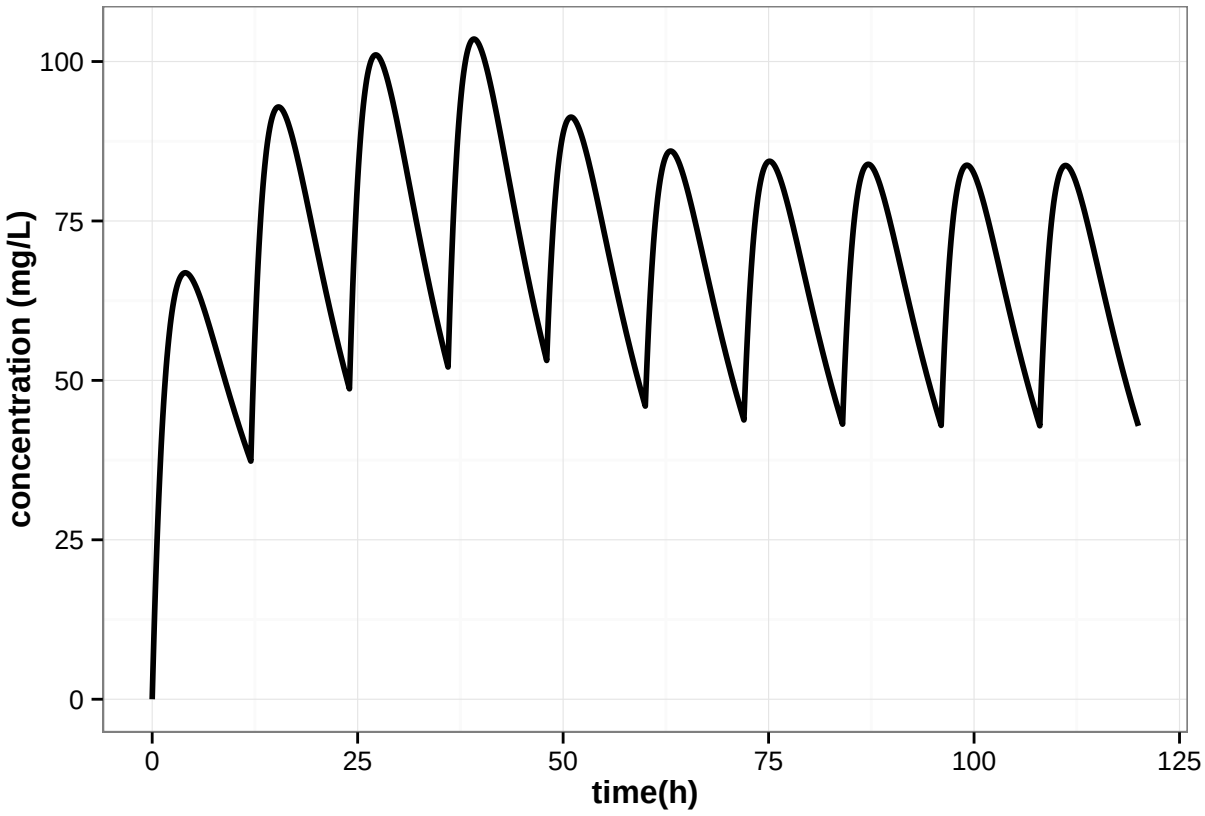
(PK profile of 100 mg oral, LD (t=0), MD (q=12 hr), CL = 0.05 L/hr, V= 1 L, ka=0.5/hr,



F=0.8)

3c. Patient consumes a high fat meal 48 hours after beginning treatment, which reduces bioavailability by 50%.

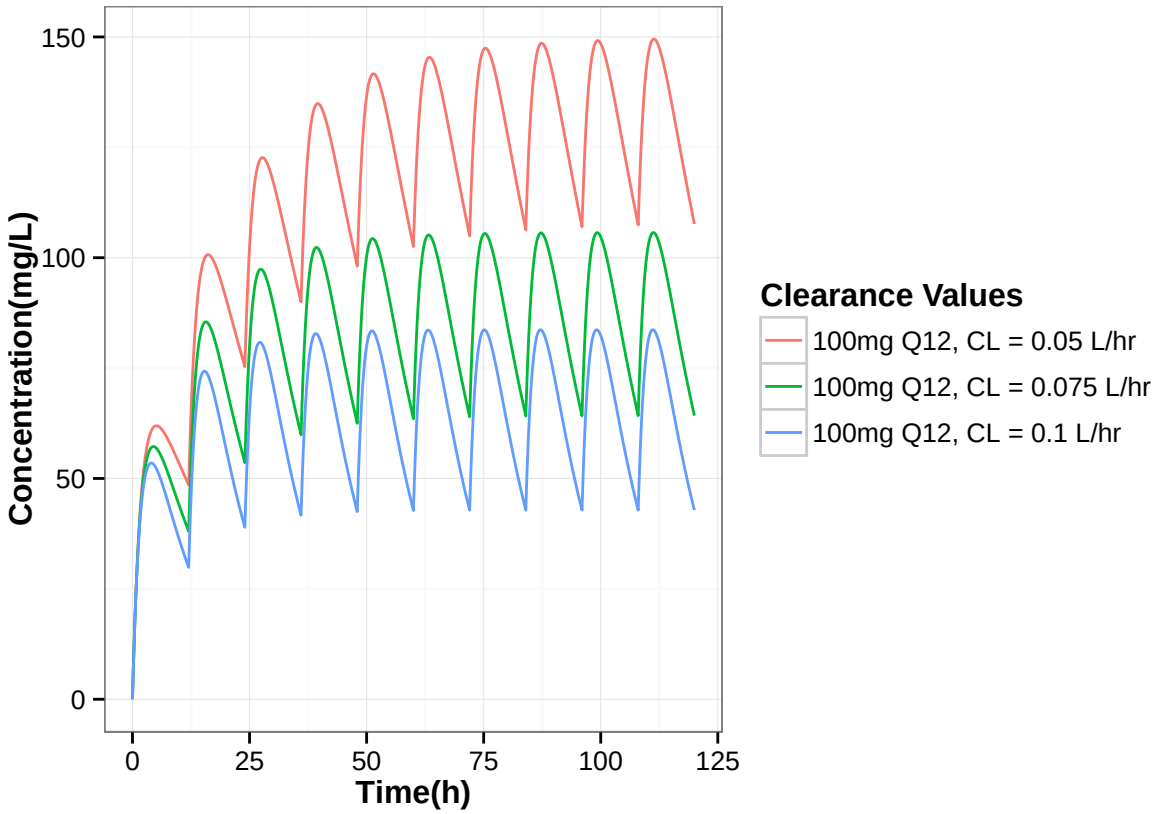
(PK profile of 100 mg oral, LD (t=0), MD (q=12 hr), CL = 0.1 L/hr, V = 1 L, ka = 0.5/hr,



F=0.4)

3d. Overlay plot of patient with decreased clearances and normal clearance.

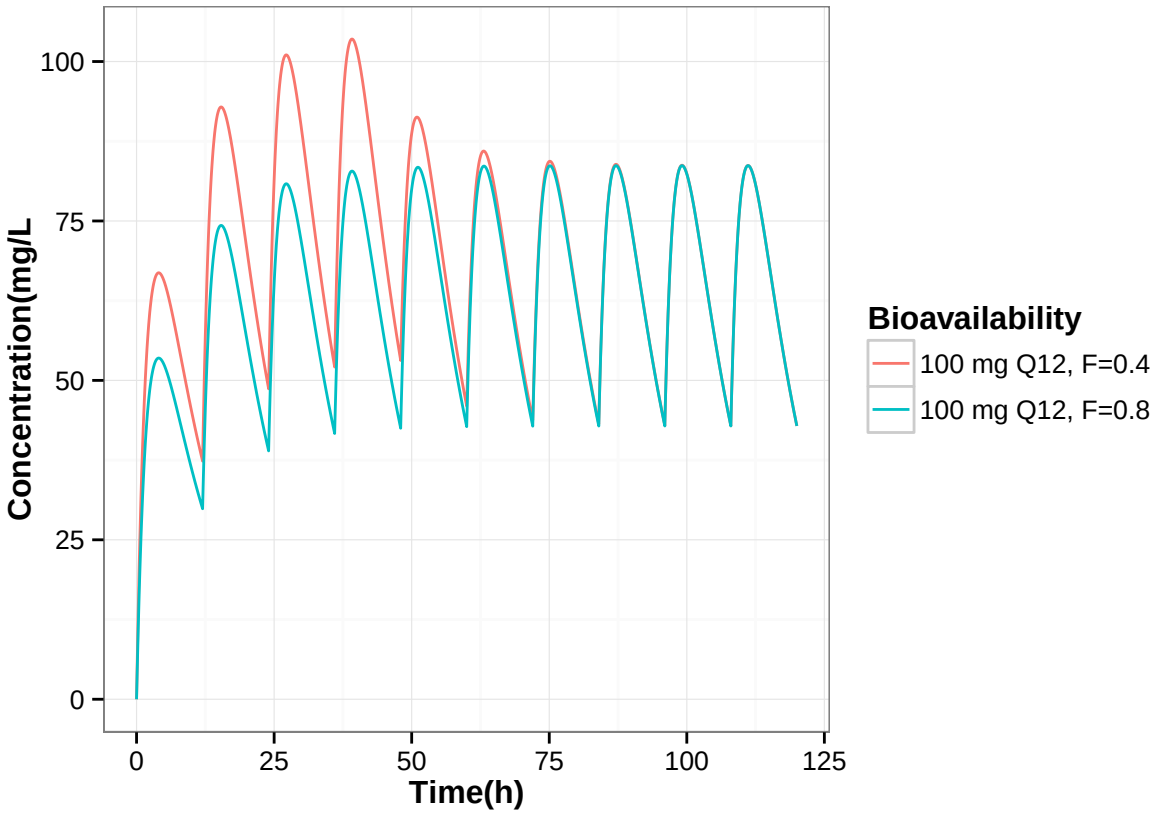
(PK profile of 100 mg oral, LD (t=0), MD (q=12 hr), CL = 0.1, 0.075, 0.05 L/hr, V = 1 L, ka =



0.5/hr, F=0.8)

3e. Overlay plot of patient with normal bioavailability and decreased bioavailability after consuming high fat meal.

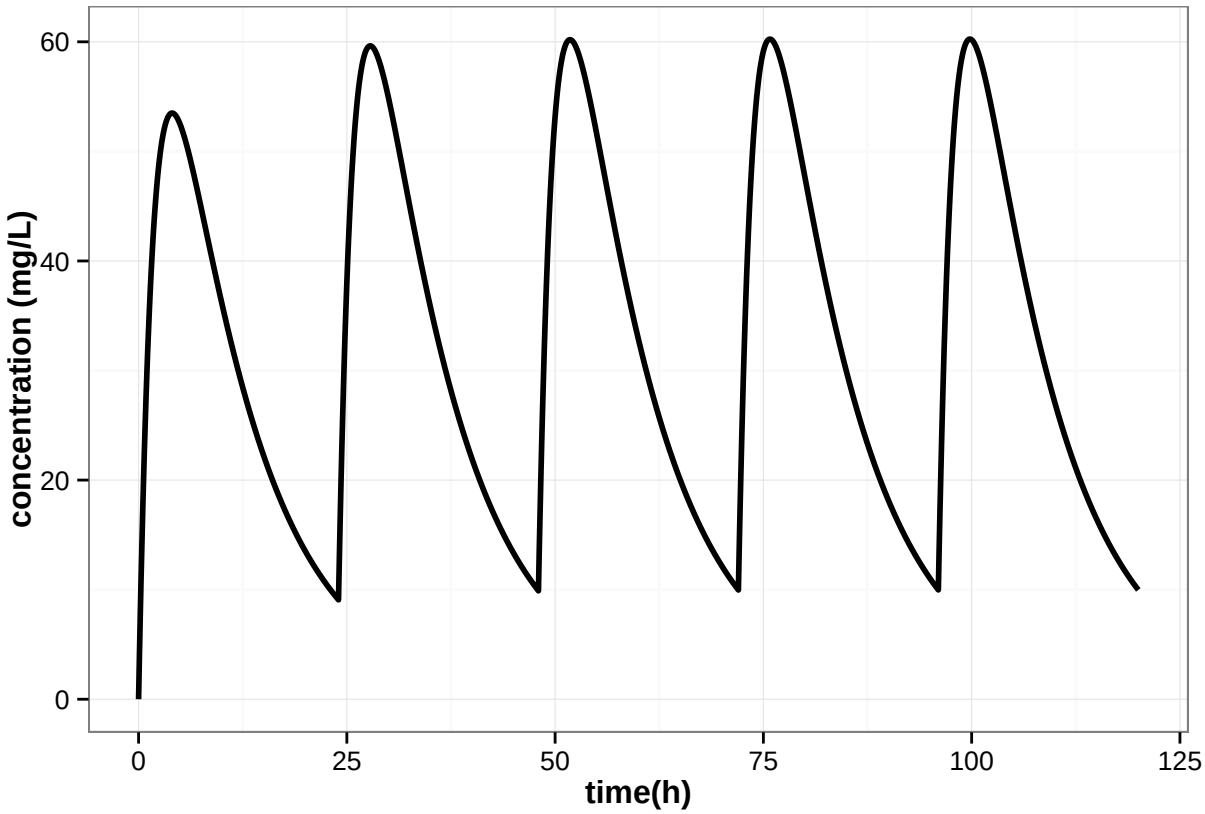
(PK profile of 100 mg oral, LD (t=0), MD (q=12 hr), CL = 0.1 L/hr, V = 1 L, ka = 0.5/hr,



F=0.8, 0.4)

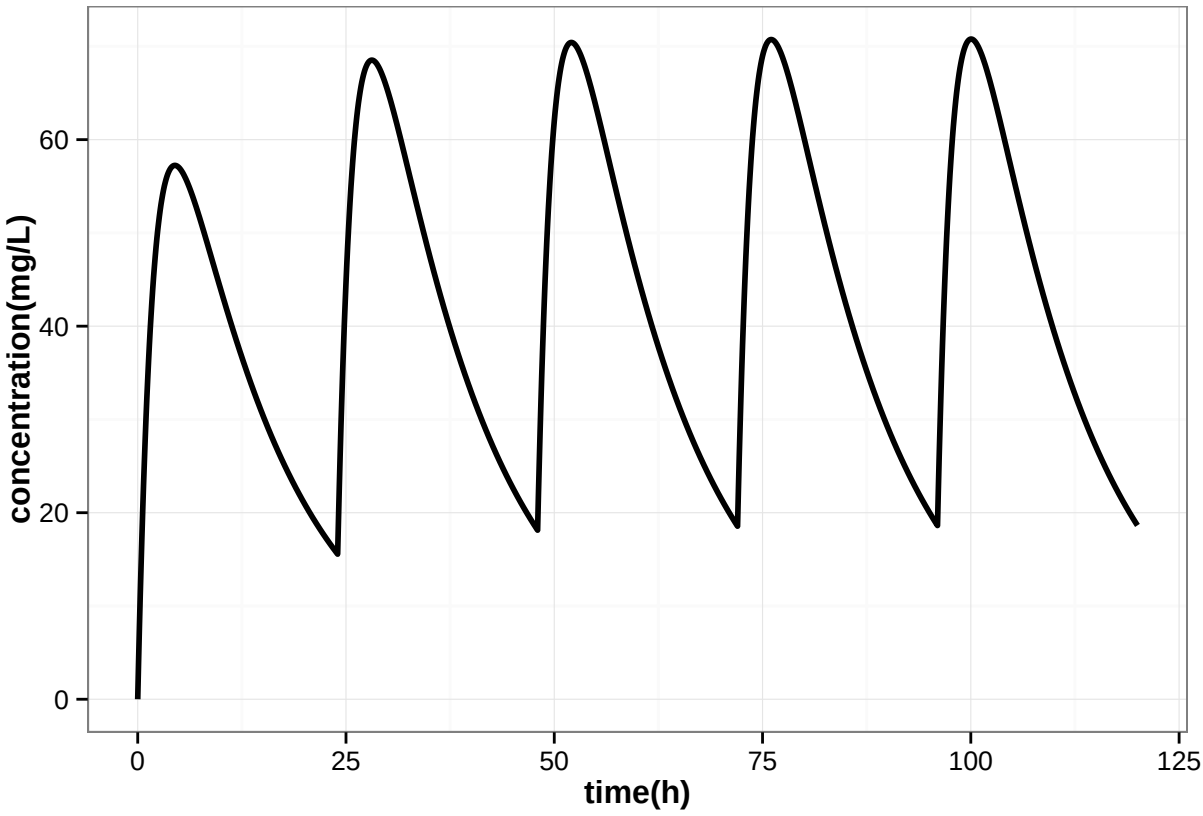
4. Patient is administered a 100 mg loading dose, followed by a maintenance dose of 100 mg every 24 hours.

(PK profile of 100 mg oral, LD (t=0), MD (q=24 hr), CL = 0.1 L/hr, V=1L, ka=0.5/hr, F=0.8)



4a. Patient's clearance decreases by 25%.

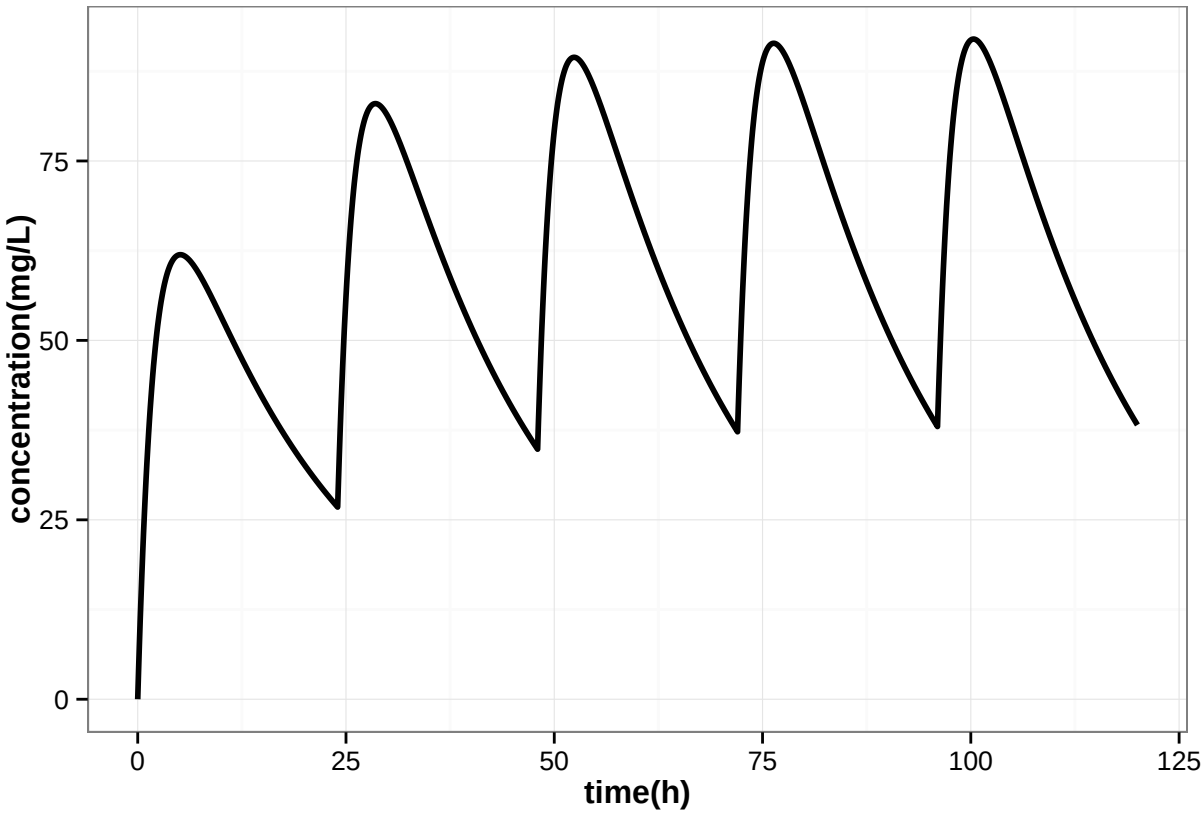
(PK profile of 100 mg oral, LD (t=0), MD (q= 24 hr), CL = 0.075 L/hr, V= 1 L, ka = 0.5/hr,



F=0.8)

4b. Patient's clearance decreases by 50%.

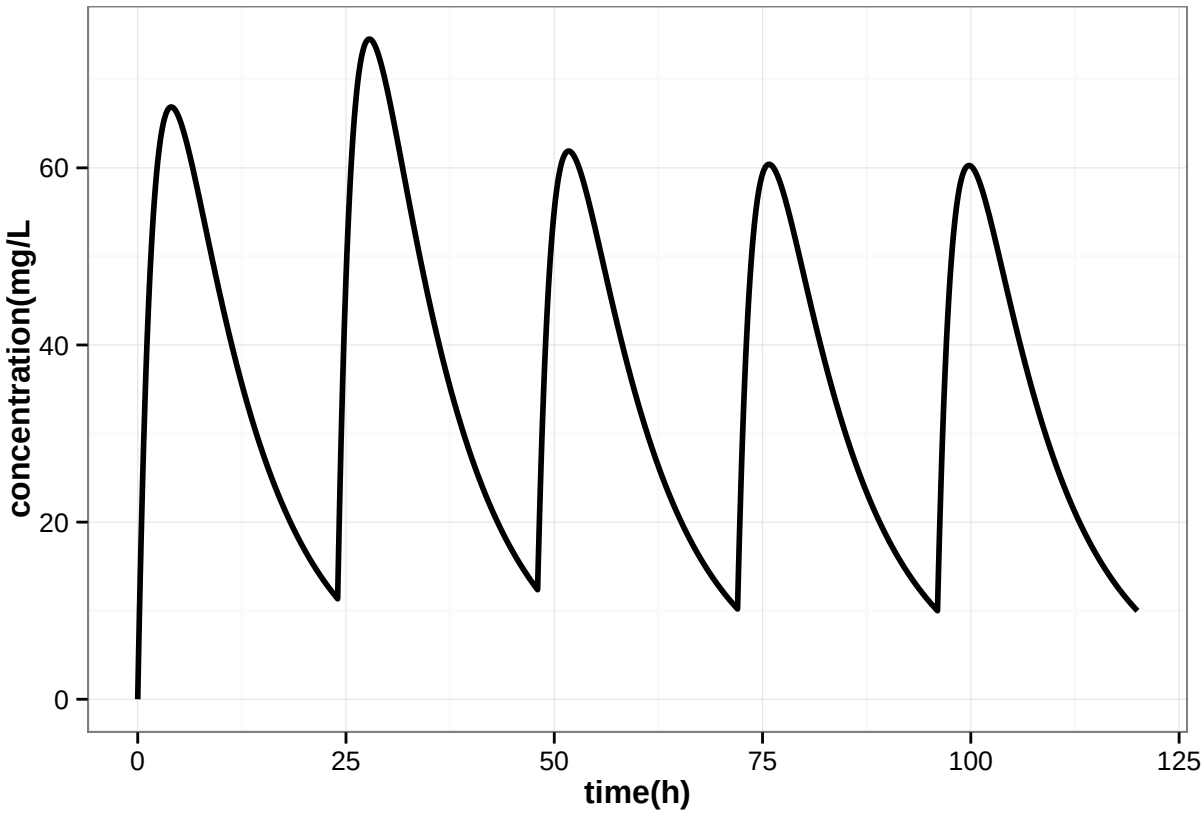
(PK profile of 100 mg oral, LD (t=0), MD (q= 24 hr), CL = 0.05 L/hr, V= 1 L, ka=0.5/hr,



F=0.8)

4c. Patient consumes a high fat meal 48 hours after beginning treatment, which reduces bioavailability by 50%.

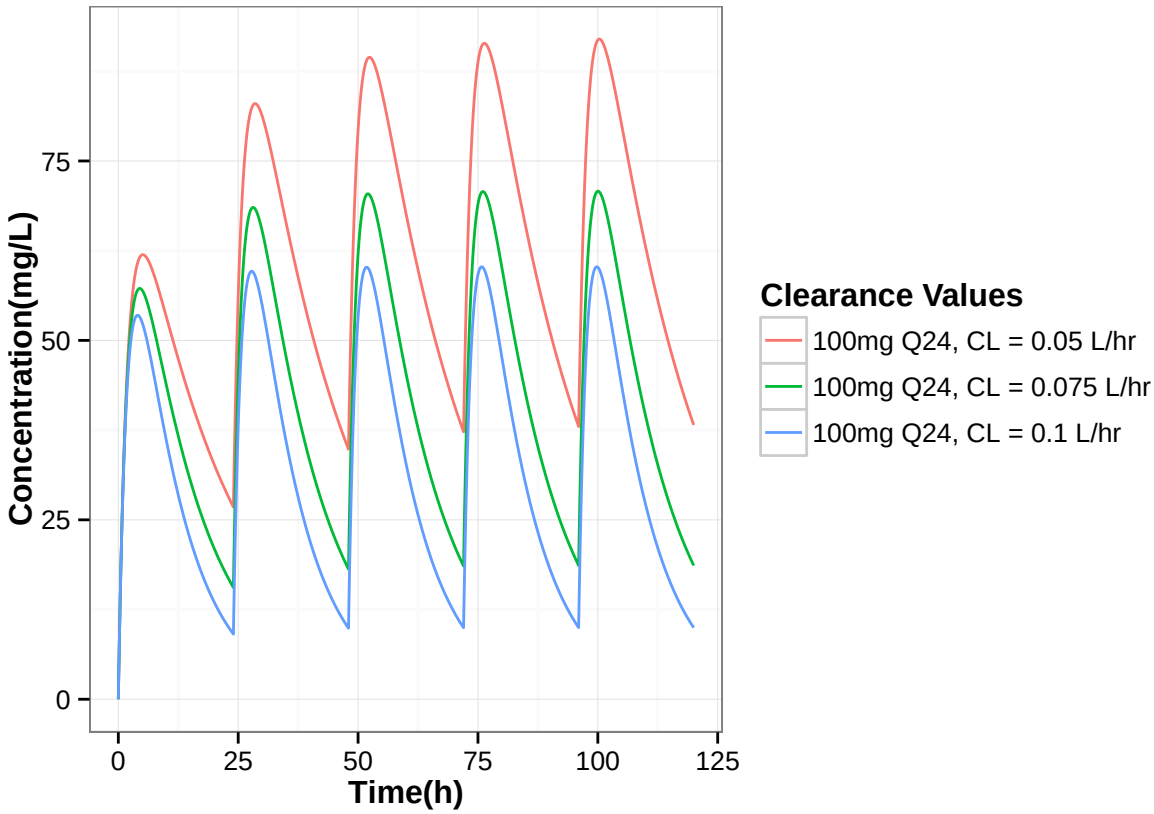
(PK profile of 100 mg oral, LD (t=0), MD (q=24 hr), CL = 0.1 L/hr, V = 1 L, ka = 0.5/hr,



F=0.4)

4d. Overlay plot of patient with decreased clearances and normal clearance.

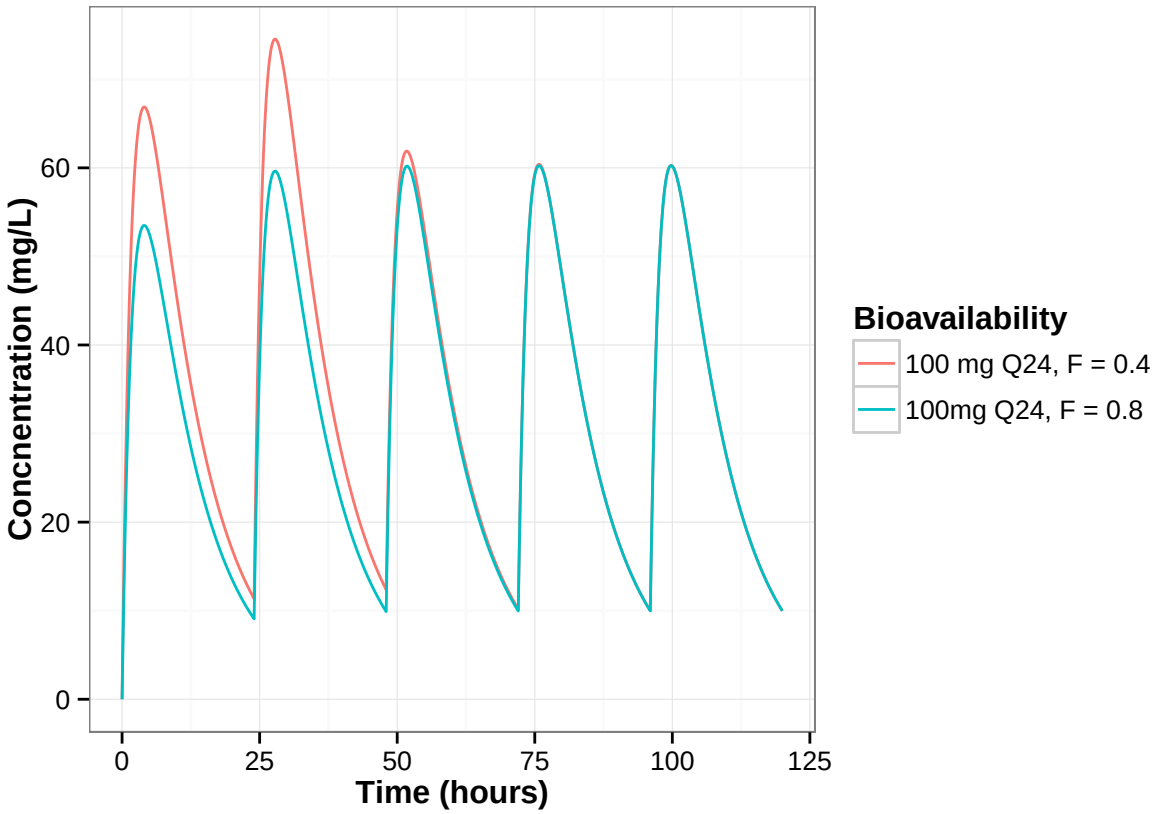
(PK profile of 100 mg oral, LD (t=0), MD (q=24 hr), CL = 0.1, 0.075, 0.05 L/hr, V = 1 L, ka =



0.5/hr, F=0.8)

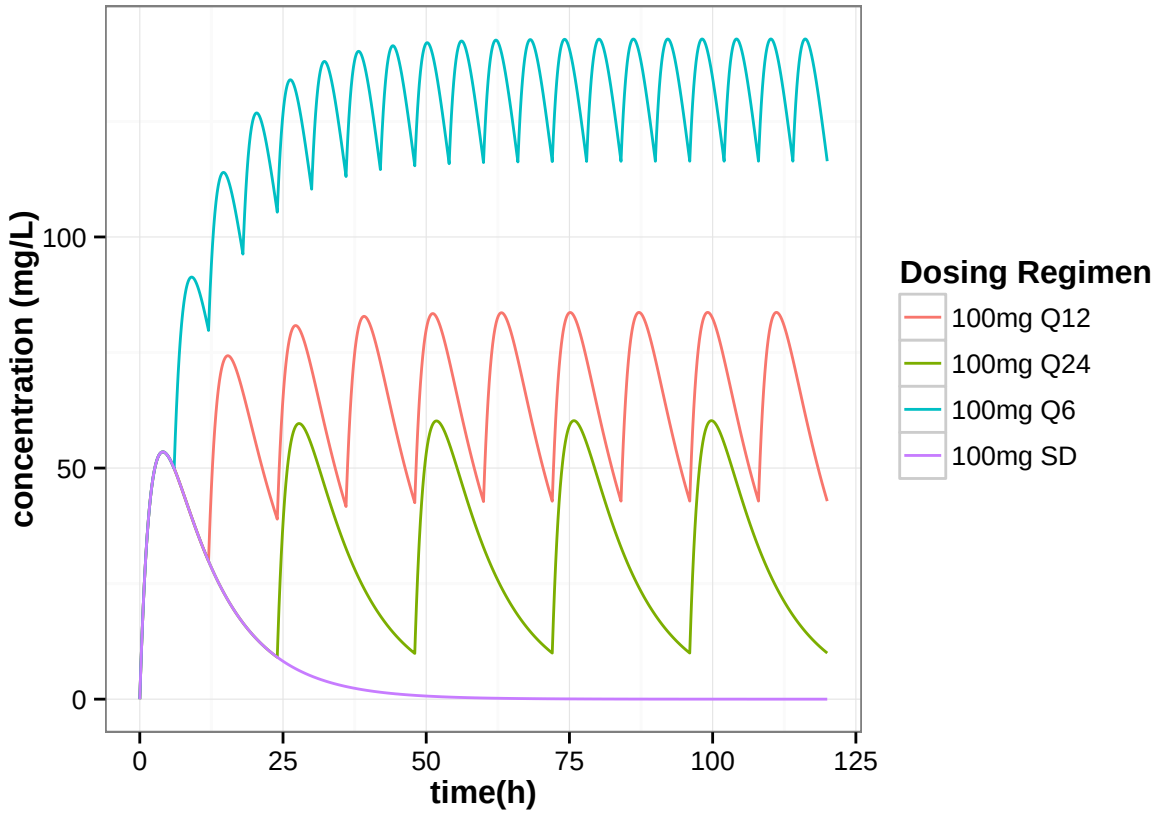
4e. Overlay plot of patient with normal bioavailability and decreased bioavailability after consuming high fat meal.

(PK profile of 100 mg oral, LD (t=0), MD (q=6 hr), CL = 0.1 L/hr, V = 1 L, ka = 0.5/hr,


Concnentration (mg/L)
0
20
40
60
0
25
50
75
100
125
Time (hours)
Bioavailability
100 mg Q24, F = 0.4
100mg Q24, F = 0.8

F=0.8, 0.4)

5. Overlay plots of all dosing intervals




```
## Session info -------------------------------------------------------------

##  setting  value
##  version  R version 3.2.2 (2015-08-14)
##  system   x86_64, darwin13.4.0
##  ui       X11
##  language (EN)
##  collate  en_US.UTF-8
##  tz       America/New_York
##  date     2015-12-09

## Packages -----------------------------------------------------------------

##  package    * version  date       source
##  assertthat   0.1      2013-12-06 CRAN (R 3.2.0)
##  colorspace   1.2-6    2015-03-11 CRAN (R 3.2.0)
##  DBI          0.3.1    2014-09-24 CRAN (R 3.2.0)
##  devtools     1.9.1    2015-09-11 CRAN (R 3.2.0)
##  digest       0.6.8    2014-12-31 CRAN (R 3.2.0)
##  dplyr      * 0.4.3    2015-09-01 CRAN (R 3.2.0)
##  evaluate     0.8      2015-09-18 CRAN (R 3.2.0)
##  formatR      1.2.1    2015-09-18 CRAN (R 3.2.0)
##  ggplot2    * 1.0.1    2015-03-17 CRAN (R 3.2.0)
##  gtable       0.1.2    2012-12-05 CRAN (R 3.2.0)
```

```
##  htmltools    0.2.6    2014-09-08 CRAN (R 3.2.0)
##  knitr      * 1.11     2015-08-14 CRAN (R 3.2.2)
##  labeling     0.3      2014-08-23 CRAN (R 3.2.0)
##  lazyeval     0.1.10   2015-01-02 CRAN (R 3.2.0)
##  magrittr     1.5      2014-11-22 CRAN (R 3.2.0)
##  MASS         7.3-44   2015-08-30 CRAN (R 3.2.0)
##  memoise      0.2.1    2014-04-22 CRAN (R 3.2.0)
##  mlxR       * 2.2.0    2015-05-31 CRAN (R 3.2.0)
##  munsell      0.4.2    2013-07-11 CRAN (R 3.2.0)
##  PKPDmisc   * 0.3.4.3  2015-10-17 Github (dpastoor/PKPDmisc@2d99b00)
##  plyr         1.8.3    2015-06-12 CRAN (R 3.2.0)
##  proto        0.3-10   2012-12-22 CRAN (R 3.2.0)
##  R6           2.1.1    2015-08-19 CRAN (R 3.2.0)
##  Rcpp         0.12.1   2015-09-10 CRAN (R 3.2.0)
##  reshape2   * 1.4.1    2014-12-06 CRAN (R 3.2.0)
##  rmarkdown    0.8.1    2015-10-10 CRAN (R 3.2.2)
##  scales       0.3.0    2015-08-25 CRAN (R 3.2.0)
##  stringi      0.5-5    2015-06-29 CRAN (R 3.2.0)
##  stringr      1.0.0    2015-04-30 CRAN (R 3.2.0)
##  XML          3.98-1.3 2015-06-30 CRAN (R 3.2.0)
##  yaml         2.1.13   2014-06-12 CRAN (R 3.2.0)
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