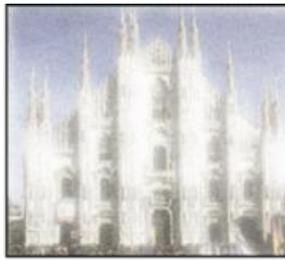




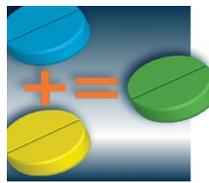
UNIVERSITÀ DEGLI STUDI
DI MILANO

DIPARTIMENTO DI
SCIENZE FARMACEUTICHE

Sezione di Tecnologia e Legislazione
Farmaceutiche Maria Edvige Sangalli

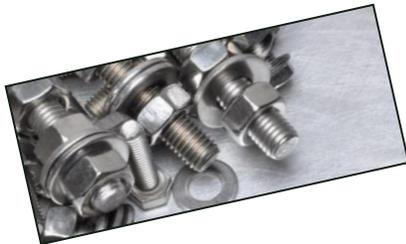


PharmTech GazzaLaB



Combinazioni a dose fissa di farmaci:
aspetti clinici, formulativi e
regolatori

*Tecnologie tradizionali ed innovative nella
fabbricazione di forme di dosaggio a
combinazioni fisse.*



Andrea Gazzaniga

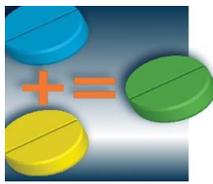


UNIVERSITÀ
DEGLI STUDI
DI MILANO

LA STATALE

Breve nota ----> nuovi sistemi e tecnologie di fabbricazione emergenti

----> elevata potenzialità di applicazione a FDC



Architettura (design) di riferimento per FDC



Core e strato esterno ----> disgregabili

Tecnica --> Press-coating



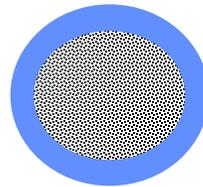
----> con lo stesso design ma obiettivi farmacocinetici completamente diversi ----> con il nome in "capa"

ChronoTopic™

M.E. Sangalli et al. JCR (2001)

----> controllo del rilascio in termini di tempo e/o sito

A. Gazzaniga et al., Eur. J. Pharm. Biopharm. (1994)



Core (compresse/capsule) a pronto rilascio contenente l'attivo

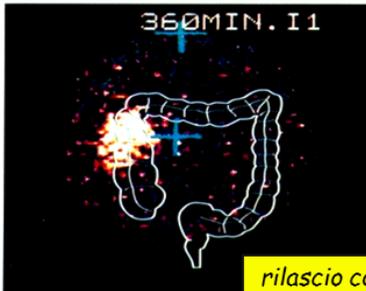
Strato esterno ----> Swellable, solubile (tipicamente HPMC 50 cps)

Tecnica --> Press-coating /solution, suspension & powder layering

rilascio ritardato

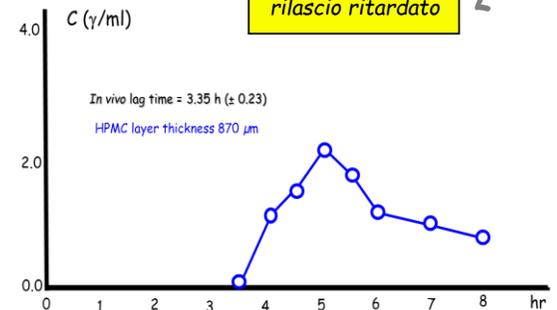


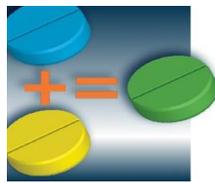
lenta interazione con fluidi biologici



rilascio colonico

---- film gastroresistente esterno ----





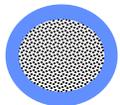
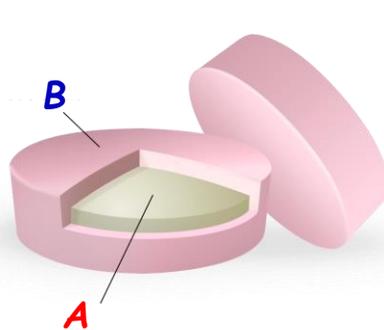
... *tenendo come schema di base*

Architettura (design) di riferimento

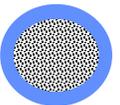
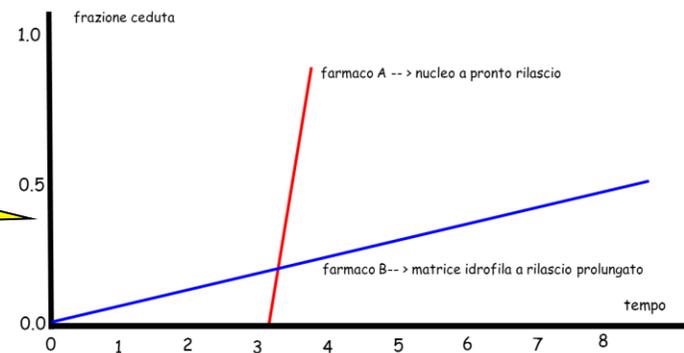
Nucleo --- > Farmaco e Formulazione **A**

Strato esterno --- > Farmaco e Formulazione **B**

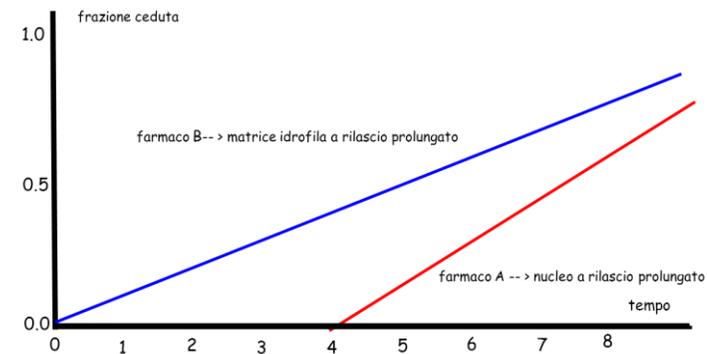
... sempre di **natura matriciale idrofila**



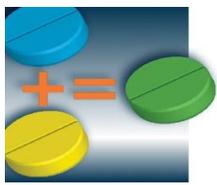
Nucleo a **pronto** rilascio (farmaco **A** compressa disgregante)
Strato esterno a rilascio **prolungato** (farmaco **B** matrice idrofila)



Nucleo a rilascio **prolungato** (farmaco **A** matrice idrofila o altro)
Strato esterno a rilascio **prolungato** (farmaco **B** matrice idrofila)



... *mantenendo come variante non trascurabile la possibilità di avere come nuclei anche capsule di gelatina dura o molle*



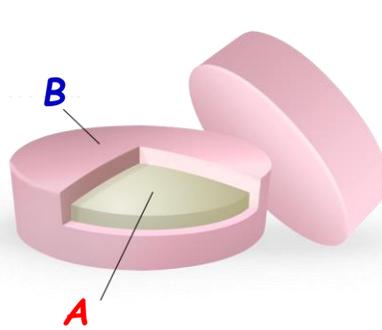
... *tenendo come schema di base*

Architettura (design) di riferimento

Nucleo --- > Farmaco e Formulazione **A**

Strato esterno --- > Farmaco e Formulazione **B**

... sempre di **natura matriciale idrofila**



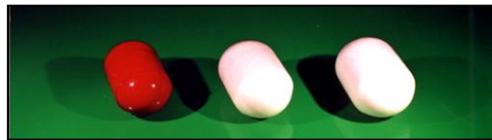
FACILE DA ALLESTIRE

MATERIALI G.R.A.S.

PROCESSI CONVENTIONALI

FABBRICAZIONE ROBUSTA

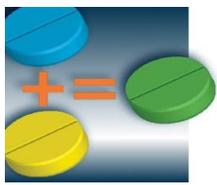
SCALE-UP GIA' SPERIMENTATO



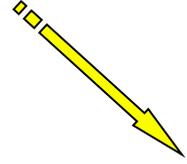
... *possibilità di veicolazione di formulazioni liquide non acquose*

... *mantenendo come variante non trascurabile la possibilità di avere come nuclei anche capsule di gelatina dura o molle*





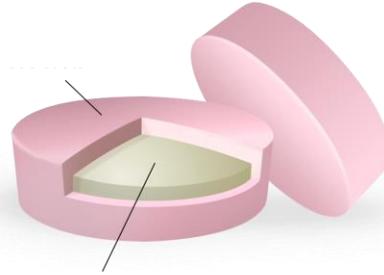
... *tenendo come schema di base*



Architettura (design) di riferimento

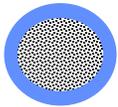
Nucleo --- > Farmaco e Formulazione **A**

Strato esterno --- > Farmaco e Formulazione **B**



... sempre di **natura matriciale idrofila**

Chronotopic™



evoluzione

da coatings funzionali --- > a shells funzionali

tecniche di layering



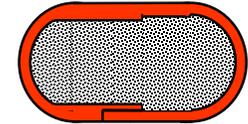
thickness μm	capacity mL
300	0.64
600	0.51
900	0.45

Thermoplastic hydrophilic swellable polymer: HPC (hydroxypropylcellulose) T_g 160-190°C

A. Gazzaniga et al., AAPS Pharm. Sci. Tech. (2011)



ChronoCap™



injection molding

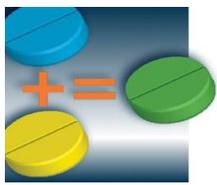


molte combinazioni possibili

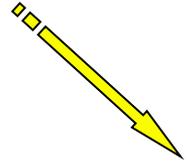


- testa e corpo cavi o pieni con farmaci e cinetiche di liberazione diverse

- filling con farmaci e formulazioni con cinetiche di liberazione diverse



... tenendo come schema di base



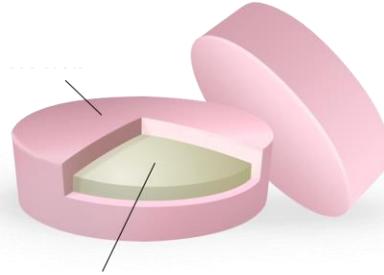
Architettura (design) di riferimento

Nucleo ---> Farmaco e Formulazione **A**

Strato esterno ---> Farmaco e Formulazione **B**



... sempre di **natura matriciale idrofila**

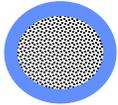


A. Gazzaniga et al., AAPS Pharm. Sci. Tech. (2011)

evoluzione

da coatings funzionali ---> a shells funzionali

Chronotopic™



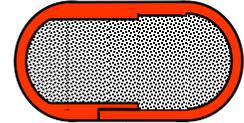
tecniche di layering



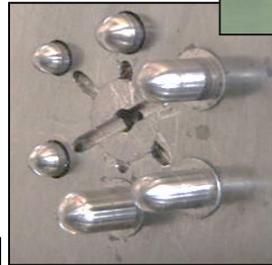
thickness μm	capacity mL
300	0.64
600	0.51
900	0.45

Thermoplastic hydrophilic swellable polymer:
HPC (hydroxypropylcellulose) T_g 160-190°C

ChronoCap™

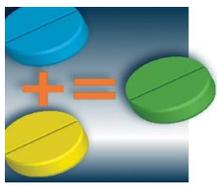


injection molding

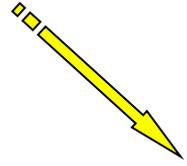


lab-scale IM press *BabyPlast 6/10P, Cronoplast, Spain*

Interessanti prospettive per CONTINUOUS MANUFACTURING



... tenendo come schema di base



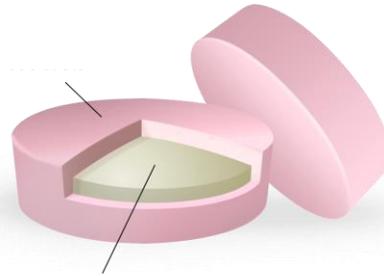
Architettura (design) di riferimento

Nucleo --- > Farmaco e Formulazione **A**

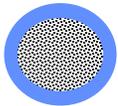
Strato esterno --- > Farmaco e Formulazione **B**



... sempre di **natura matriciale idrofila**



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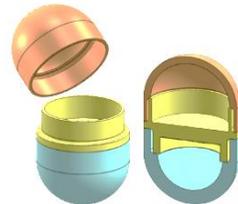
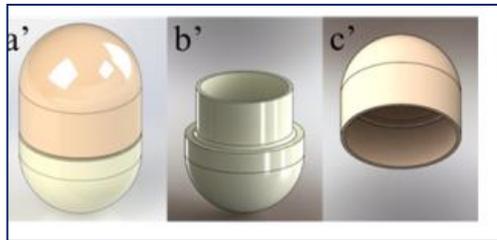
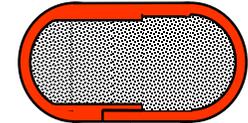
evoluzione

da coatings funzionali --- > a shells funzionali

A.Melocchi et al., *J Drug Deliv Sci and Technol* (2015)

L. Zema et al. *J Pharm Sci* (2017)

ChronoCap™

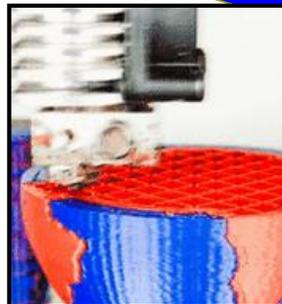


3D printing

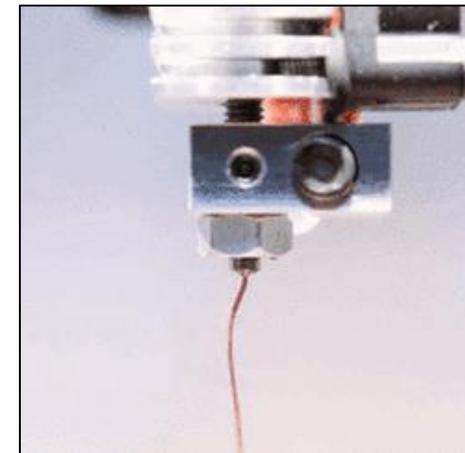
ulteriore evoluzione

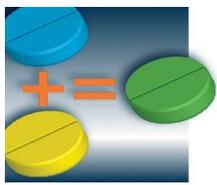


Thermoplastic hydrophilic swellable polymer:
HPC (hydroxypropylcellulose) T_g 160-190°C



A.Maroni et al., *J.Contr. Release* (2017)



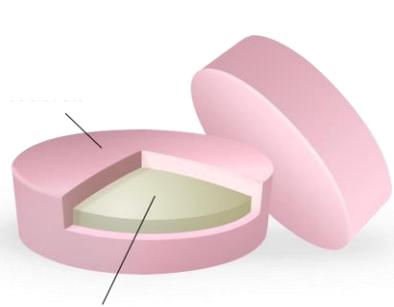


... tenendo come schema di base

Nucleo --- > Farmaco e Formulazione **A**

Strato esterno --- > Farmaco e Formulazione **B**

Architettura (design) di riferimento



... sempre di **natura matriciale idrofila**



notopic™

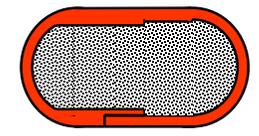
TechLab

evoluzione

A.Melocchi et al., *J Drug Deliv Sci and Technol* (2015)

L. Zema et al. *J Pharm Sci* (2017)

ChronoCap™



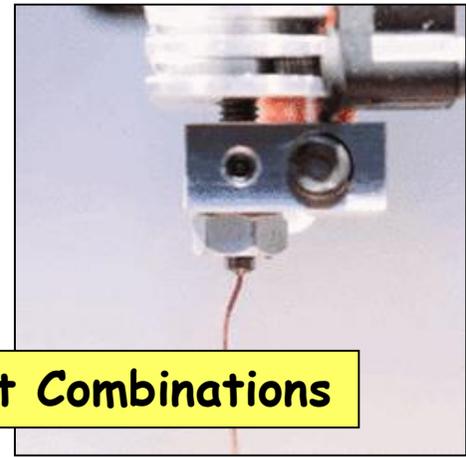
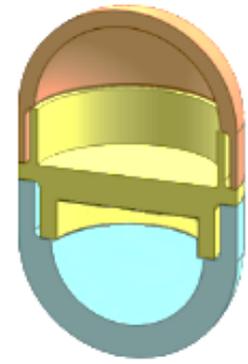
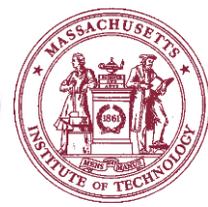
da coatings funzionali --- > a shells funzionali

3D printing

A.Maroni et al., *J.Contr. Release* (2017)

Start-up

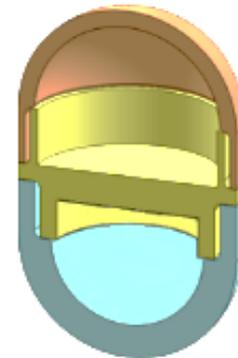
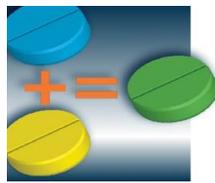
UNIMI / M.I.T.



MultiplyLabs

MULTICOMPARTMENT Capsular device for SUPPLEMENTS

FSC - Fixed Supplement Combinations



PharmTech GazzaLaB

MULTICOMPARTMENT
Capsular device for SUPPLEMENTS

FSC - Fixed Supplement Combination