
OSMOPHARM S.A.
Pharmaceutical modified release products
A Swiss pharmaceutical company specialised in oral modified
drug delivery systems under contract manufacturing
www.osmopharm.com

WELCOME

Presentation

Osmopharm is a Swiss pharmaceutical Company. Created in 1994, it is specialised in modified release systems for oral drugs, based on the application of some of the more advanced galenic technologies.

Osmopharm's major activity is the production under contract manufacturing by following the more strict GMP rules assured by Swissmedic and by prestigeous pharmaceutical companies inspection.

Its technical management, with about 40 years of experience, can study and develop new products offering to the costumers a global support for new registrations and/or for actualizing the existing ones by according to regulatory requirements.

Osmopharm staff is composed by about 100 persons that, in order to meet the customers expectations, is under a continuous challenge for studying new technologies and formulations and to maintain the highest Quality Levels.

Osmopharm is located in Southern Switzerland, a few km north of Lugano and 70 km from Milan.

The total covered surface, exterior warehouses comprised, is about 6.000 sqm.
The production is distributed in 43 working rooms, granting a high flexibility and capacity.

With more than 150 different formulations, the monthly production is today nearly to 120 millions capsules/doses/tablets (corresponding to about 350 tons/year).
Indeed, the potential capacity could be increased to 200 millions/month, by working on double shift (presently 1 shift).

Osmopharm can sell in bulk but also producing capsules, tablets and, upon request, can blister and package them, providing its clients, by this, a full service from API procurement to final for pharmacy presentations.

Market & Evolution

Osmopharm became, during the years, one of the worldwide leaders contract manufacturers in its field.

Today Osmopharm's pharmaceutical customers are over 100, most of them very prestigious.

The sales are worldwide distributed in more than 30 countries;
the main market is Europe followed by north Africa, Asia, south and central America

Being Europe its main market, Osmopharm SA is committed to respect Swiss and European community rules.

Osmopharm's market goal is to enlarge its presence in the already existing markets and to enter in new ones.

In the shortest time, Osmopharm intends to register new dossiers by investing into new bioequivalences studies.

Quality

Osmopharm SA is authorised by the Swiss National Health Authorities (Swissmedic), considered among the strictest in the world, to comply with the current GMP requisities in the manufacture of pharmaceutical products according to the Swiss regulations in force, matching customer's highest expectations.

These regulations are in accordance with the requirements for good practices in the manufacture and Quality control of the Pharmaceutical Inspection Convention/Co-Operation Scheme (PIC/S) and the Directives of the European Commission.

The respect of the current EU GMP rules is assured also by the prestigeous pharmaceutical companies inspections and by Osmopharm's team, very experimented, that is the instrument for reaching and increasing the quality levels.

Moreover, a top class quality control equipment allows the application of a wide experience and deep professionality.

Synthetic data

SWISS PRODUCTION SITE:
south Switzerland, in Bedano near Lugano.
About 70 km North from Milano.

PERSONNELS:
about 100 employees

CERTIFICATION:
cGMP issued by Swissmedic

ACTIVITY:
under contract manufacturing production of modified release solid oral form in pellets, tablet or resinate dispatched in bulk. If requested, capsule filling and/or blistering and/or packaging for pharmacy is feasible.

ADVANCED TECHNOLOGIES:
coating-pans, Extrusion-spheronisation, Ion-Exchange resinates

FINAL DOSIFICATION:
hard gelatine capsules or tablets

CAPACITY:
today with one shift, about 120 millions doses monthly equivalent to about 1.4 billions doses or 350 tons/yearly.

POTENTIAL CAPACITY:
with double shift, about 200 millions doses monthly.

REGULATORY ACTIVITIES:
supports the clients with the preparation of new dossiers and up to date of existing ones following regulatory requisities in CTD format.

R&D:
more than 40 years of experience in our field, new development related activities (study, development, scale up production, validations and stability) to collect data to generate the CTD dossier (technical part) for registration purposes.

Pellets

PELLETS Pellets type A
Coating-pan technology
Osmopharm`s main kind of product is presented in pellet form: spherical granules of about 1 mm diameter. These granules can either be dosed in hard gelatine capsules or be directly compressed to obtain sustained release tablets. Capsules filling or tabletting can be performed by Osmopharm or by the customers. For tabletting, no other work is required for the customer than to regulate the machine (direct compression). Special coating-pans are the mainly used machines for Osmopharm products. These machines are about 40, whose global capacity is about 12.000 liters.

Physical Production Principle
Granules are created by continuous rotation into the pan and risen by application of active principles and excipients over a starting inert granule. Generally, at the end of the process they are coated with a porous membrane that covers the core. The release is regulated by the thickness and solubility of the membrane on parallel with the complexity of the core matrix.

Pellets type B
Extrusion-spheronisation technology
This technology, generally called "Marumeriser", allows to create pellets (with complex matrix as well).

Compared to coating-pan technology:
Advantages:
- Higher speed of production for high potency products.

Disadvantages:
- The physical appearance and shape of the pellets is sometimes less regular than those with coating-pan machine.
- Impossibility to create multi layered complex matrix.

Physical Production Principle
- Active principles and excipients are homogenized in a planetary mixer.
- The mass is passed through a special granulator with the production of a "spaghetti" shaped mass.
- Finally, a special centrifuge cut the filamentous mass, obtaining spherical granulates.
- The exterior membrane coating is obtaining by a coating-pan machine.

ION-exchange resinates

The ion-exchange resinates are obtained by using special enamelled reactors.

Taste Masked Syrups
This technology is used for the creation of modified release forms, nevertheless a very specific application is for masking the unpleasant taste of some active principles.
These can be transformed in resinates and suspended in a no taste syrup.
After ingestion, the gastric acid will free the active principle for a normal or contolled activity.

Some principles of Chemistry
Ion-exchange resins are polymers presenting linked ionisable groups (generally weak acids or bases). In case of cationic resins, the protons can be replaced by other molecules having the same charge.
For example, by using a cationic resin, its H+ can be replaced by a positive ionisable group of a raw material in it chloridrate form, creating a new compound: a resinate. This new compound, stable at neutral pH, will free the active molecule when, after ingestion, reaches the gastric HCl solution.

Blistering and Packaging

Since October 2004 Osmopharm has implemented his line production with a new department of blistering, putting in flasks and packaging in cases.
With such operation, Osmopharm offers his worldwide customers a complete service from development and production to finished products, always respecting highest expectations of quality standards and GMP.

BENEFITS

General properties

Modified release oral dosage forms are becoming increasingly important, either to achieve the desired level of therapeutic activity required for a new drug or to extend the life cycle of an existing one.

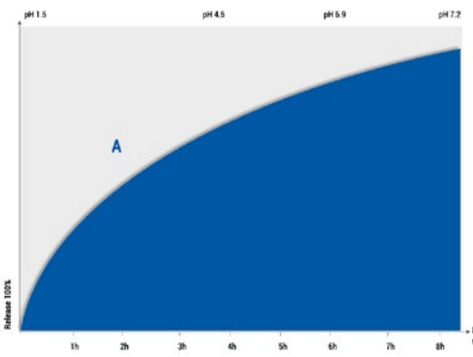
These technologies can be applied to many pharmaceutical formulations which, by providing modulated absorption may reduce oral administration of a medicament to only one or two daily doses (see curve in example A: in vivo controlled release of a pharmaceutical active substance).

This explains why modified release oral specialties are strongly recommended in all cases where patients are obliged, for the short half-life of a drug, to ingest several doses daily.
See Graphic N° 1

Other two examples:
The first one shows how there is a reduction of secondary effects when administering the delayed form.
See Graphic N° 2

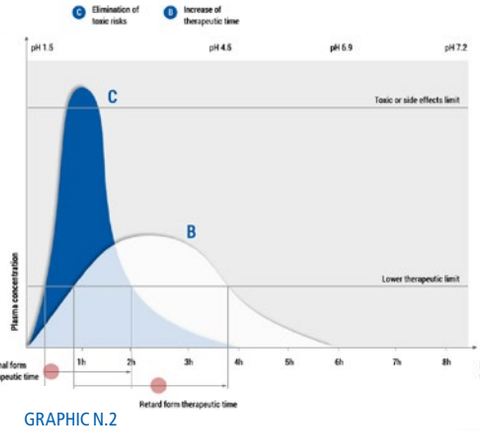
The second example shows patient convenience of administering only one delayed single dose (B) instead of four normal doses (C).
See Graphic N° 3

DISSOLUTION PROFILE



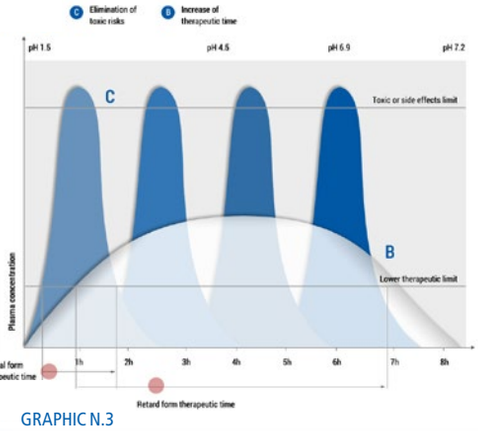
GRAPHIC N.1

FIRST EXAMPLE: SAME DOSAGE



GRAPHIC N.2

SECOND EXAMPLE: SAME DOSAGE



GRAPHIC N.3

PH variation dependence

To ensure constant clinical effectiveness of orally administered medicaments, its absorption should be as independent as possible from physiological variables of the human body.
One of these variables is the pH level of the gastrointestinal tract, which can affect the release of active substance contained in a pharmaceutical preparation.
Osmopharm's technology can reduce this variability without modifying the chemical structure of the active substance providing, even in different pH conditions, a more constant release.

Advantages and disadvantages

A short half-life time of the medicament and its active metabolites oblige the patient to take many doses a day.
A calculate release dissolution of the medicament compensate the clearance of the active principle maintaining the therapeutic activity desired for a long time.

Absorbtion peaks risks in normal galenical forms should be avoided by paying attention to the over dosages.
A reduced but constant release of the active principle can eliminate any dangerous peak.

Some medicaments are destroyed by gastric acidity. Thanks to a gastro-enteric coating, the medicament is protected until its arrival into the duodenum.

Gastric irritation or sensation of heaviness in the stomach are strongly reduced with a multiparticulated form as.

Big variation on the speed of the gastro-intestinal tractus passage with consequent variation of therapeutic effects is avoided because the passage time through the gastro-intestinal tractus becomes more homogeneous.

Multi-particule dosage forms

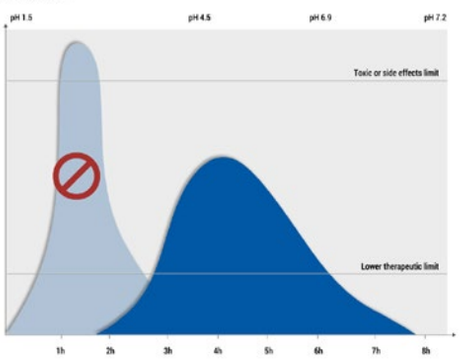
Mono-dosed sustained release medicaments (tablets) stop at certain sites irritating the mucosa: the release can be reduced and medicaments not fully absorbed.
Osmopharm's 1-1,2 mm sized spherical pellet granules assure a rapid and homogeneous spread of the medicament in the gastrointestinal tract avoiding those risks.

Gastric Protection

Many pharmaceutical active substances are sensitive to the gastric juice acidity. By protecting these active substances with pH sensitive polymeric membrane coatings (insoluble to pH 1-2 levels and soluble at higher pH levels), Osmopharm's technology provides these active substances with strong acid protection (more than two hours in gastric acid), followed by high enteric juice release.

THIRD EXAMPLE:

enteric coating for gastric protection



GRAPHIC N.4

PRODUCT LIST

Osmopharm SA

Via alle Fornaci
6930 Bedano
Switzerland

Tel. +41(0)91 935 20 40
Fax +41(0)91 935 20 49

osmopharm@osmopharm.com
www.osmopharm.com