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Multiple Unit Pellet System (MUPS): A Comprehensive Review of Formulation Approaches, Evaluation, and Emerging Applications in Oral Drug Delivery

Samir Sarju Chavhan[1] and Dr. Amol A. Harsulkar [2]
M.Pharm Scholar, Research Guide, Department of Industrial Pharmacy[1,2]
Sudhakarrao Naik Institute of Pharmacy, Pusad
Sant Gadge Baba Amravati University, Maharashtra, India

Abstract: *Conventional single-unit oral dosage forms such as tablets and capsules continue to dominate pharmaceutical therapy, yet they carry inherent drawbacks — irregular gastric emptying, unpredictable plasma drug profiles, and the possibility of catastrophic dose dumping if the unit fails. The Multiple Unit Pellet System (MUPS) addresses these shortcomings by dividing the dose across a large population of small, discrete pellets that are subsequently encapsulated or compacted into a single dosage unit. On administration, the pellets disperse independently across the gastrointestinal tract, which smooths out absorption, lowers the odds of localized mucosal damage, and confines the consequence of any single pellet's failure to a fraction of the total dose. This review consolidates current understanding of MUPS technology, covering its rationale and classification, the excipients and pelletization routes (extrusion-spheronization, layering, and hot-melt extrusion) used to build it, the parameters by which pellet quality is judged, coating strategies for enteric and sustained-release performance, the mechanisms governing drug liberation from coated pellets, representative marketed products, and the manufacturing and scale-up obstacles that still limit wider adoption. Emerging directions — including nanoparticle-loaded pellets, Quality-by-Design-driven process control, and chronotherapeutic and colon-targeted coatings — are also discussed, alongside the outlook for MUPS as a platform for individualized, modified-release oral therapy.*

Keywords: *Multiple Unit Pellet System, Multiparticulate Drug Delivery, Pelletization, Extrusion-Spheronization, Enteric Coating, Sustained Release, Controlled Drug Delivery, Oral Formulation*

I. INTRODUCTION

Oral administration remains the most common and most favoured route for delivering medicines, largely because it is inexpensive, non-invasive, and easy for patients to manage on their own. Yet the conventional single-unit forms built around this route — a single tablet core or a single capsule shell — behave, pharmacokinetically, as one indivisible packet of drug. Because that packet empties from the stomach as a whole and travels the gut as a whole, its performance is tied to the fate of one physical object: if it lodges too long at one site, or if its coating cracks prematurely, the entire dose is affected at once.

Multiparticulate technology was developed specifically to break that dependency. Instead of one large unit, the dose is divided among hundreds or thousands of small pellets, so that no single point of failure can compromise the whole formulation. Among the various multiparticulate strategies, the Multiple Unit Pellet System (MUPS) — pellets either packed into capsules or compressed into a tablet — has become the most industrially established, and is the focus of this review.

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Table I contrasts the behaviour of conventional single-unit dosage forms with that of MUPS across the properties that matter most in formulation and clinical use.

TABLE I

COMPARISON OF CONVENTIONAL SINGLE-UNIT DOSAGE FORMS AND MUPS

Parameter	Single-Unit Dosage Form	MUPS
Basic unit	One tablet or capsule carries the entire dose	Dose is spread across many small pellets housed in a tablet or capsule
Typical examples	Conventional tablet, conventional capsule	Pellet-filled capsule, compressed MUPS tablet
Site of drug release	Concentrated at one location in the GIT	Distributed across multiple sites in the GIT
Dose-dumping risk	Higher — failure affects the whole dose	Lower — failure of a few pellets is diluted across the rest
Gastric emptying pattern	Can be irregular and food-dependent	More uniform and predictable
Plasma concentration profile	Greater peak-to-trough fluctuation	Comparatively steady
Local mucosal irritation	More likely	Reduced
Patient compliance	Adequate	Generally better for modified-release therapy
Control over release pattern	Limited	Flexible and better controlled
Formulation complexity	Simple	More elaborate
Manufacturing cost	Lower	Higher
Consequence of unit damage	Entire dose compromised	Only the affected pellets are compromised
Bioavailability	Can be variable	Generally more reproducible
Best suited for	Immediate-release products	Sustained, delayed, and enteric-coated release

A MUPS unit is, at its core, a multiparticulate carrier: numerous spherical subunits, each independently capable of holding drug in immediate-release, sustained-release, delayed-release, or enteric-coated form, that are brought together into one capsule or tablet at the point of manufacture. Because these subunits scatter through the stomach and intestine independently of one another, the surface area available for absorption is larger and more evenly presented than with a single monolithic unit, and the drug-release outcome becomes considerably easier to predict.

This subdivision of the dose is also what gives MUPS its principal safety advantage. Where a single-unit sustained-release tablet risks releasing its entire payload at once if its coating is breached, a MUPS formulation loses only the output of the damaged pellets — the rest continue to perform as designed. That property is especially valuable for potent drugs and for narrow-therapeutic-index actives formulated for modified release.

Individual pellets typically measure between 0.5 mm and 1.5 mm and, owing to their spherical geometry and smooth surface, flow well during processing — a property that simplifies both capsule filling and tablet compression without compromising pellet integrity. The same uniform dispersion that improves absorption also reduces the local drug concentration presented to the gastric mucosa at any one point, easing the irritation risk associated with some actives.

Because gastric emptying of pellets is less tied to the fed or fasted state than that of a single large unit, MUPS formulations tend to show smaller inter- and intra-subject variability in absorption, translating into steadier plasma concentrations and more consistent bioavailability. The format also lends itself to combining pellet populations with different release characteristics within one dosage form, opening the door to combination products and multi-phase release profiles.

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Several manufacturing routes — extrusion-spheronization, solution or suspension layering, powder layering, and hot-melt extrusion — are used to build the pellets themselves, with extrusion-spheronization the most widely adopted owing to its ability to deliver narrow size distributions and mechanically robust pellets at industrial scale. The remainder of this review examines the formulation science, evaluation methodology, coating strategies, release mechanisms, applications, and outstanding manufacturing challenges associated with MUPS technology.

II. OVERVIEW OF MULTIPLE UNIT PELLET SYSTEM (MUPS)

A. Definition of MUPS

MUPS refers to an oral dosage form built from a large number of small, discrete pellets that are packed into a capsule shell or compacted into a tablet, so that the finished product behaves, in aggregate, as a single dose while its internal architecture remains multiparticulate. Depending on the therapeutic need, individual pellets may be designed for immediate, sustained, delayed, or enteric release.

Because drug is distributed among the pellet population rather than concentrated in one core, absorption tends to be more consistent and the dosage form is inherently more forgiving of localized manufacturing defects. Dose dumping — a real risk when a single-unit coating fails — is substantially attenuated, since only a subset of pellets is affected by any one defect.

The technology has been adopted widely across the industry precisely because it allows formulators to mix pellet populations with different release profiles inside one dosage form, making it a natural fit for sustained-release, delayed-release, and site-specific delivery objectives.

B. Multiparticulate Drug Delivery: The Broader Concept

MUPS sits within the larger family of multiparticulate systems, which also includes granules, beads, microspheres, and mini-tablets — all of them dosage forms built from many small units rather than one large one. What unites the family is the way these units disperse through the gut after administration, spreading the dose more evenly than a single-unit form ever could.

The rationale for adopting a multiparticulate approach traces back to the specific weaknesses of single-unit systems: uneven gastric emptying, unpredictable release, transient high local drug concentrations, and dose-dumping risk. Subdividing the dose directly counters each of these — the impact of any one unit's failure is proportionally small, which is itself a meaningful safety margin.

Multiparticulate systems also give formulators room to tailor the release profile precisely, since different coatings or polymer blends can be applied to different sub-batches of pellets and then recombined. This flexibility extends to combining otherwise incompatible actives in the same dosage form, each isolated within its own pellet population, and to reducing dosing frequency by engineering a controlled, extended release — both of which support better patient adherence.

III. ADVANTAGES OF MUPS

MUPS technology offers several formulation and clinical advantages over conventional single-unit tablets and capsules, largely stemming from the way the dose is distributed across many independent pellets.

A. Uniform Drug Distribution

Because pellets disperse throughout the stomach and intestine rather than lingering at one site, the effective surface area available for absorption is larger, and release becomes considerably more predictable. This also smooths out variability in gastric emptying and dampens the swings in plasma concentration that single-unit forms are prone to, ultimately supporting better bioavailability and therapeutic response.

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B. Reduced Risk of Dose Dumping

Dose dumping — the uncontrolled, premature release of most or all of a drug load — is a recognized hazard of single-unit sustained-release products whose coating is damaged. Spreading the dose across many pellets contains this risk: even if a subset of pellets is compromised, the remaining population continues to release drug as intended, which matters most for potent or narrow-therapeutic-index actives.

C. Reduced Gastric Irritation

Because the drug load is spread thin across many independently dispersing pellets rather than concentrated at one contact point, the local drug concentration at the gastric mucosa at any given moment is lower than with a conventional tablet. This is particularly useful for actives known to irritate or damage the stomach lining.

D. Improved Patient Compliance

By engineering sustained or controlled release, MUPS formulations reduce how often a patient needs to dose, which in practice improves adherence. The smoother plasma-concentration profile that typically results also tends to reduce side effects, further supporting patient acceptance of the therapy.

IV. DISADVANTAGES AND LIMITATIONS OF MUPS

- The benefits of MUPS technology come at the cost of a more demanding manufacturing process, and several practical limitations continue to constrain its use.
- Complex manufacturing: pellet formation, coating, drying, and (for tablet-based systems) compression are all separate unit operations, each requiring specialized equipment; small deviations at any stage can alter release performance.
- Higher production cost: the equipment, coating materials, and skilled operators required push manufacturing costs above those of conventional tablets and capsules.
- Pellet damage on compression: tablet-based MUPS pellets can crack or deform under compressive force, disturbing the coating and altering the intended release pattern unless cushioning agents and compression force are carefully optimized.
- Uneven coating: differences in individual pellet size and shape make it difficult to apply perfectly uniform coating thickness, and any unevenness translates directly into inconsistent drug release.
- Segregation during processing: pellets of differing size or density can separate during mixing or filling, producing dose variability and poor content uniformity.
- Storage stability concerns: moisture and temperature exposure can compromise coated pellets, which is a particular concern for moisture- or heat-labile drugs.
- Scale-up difficulty: reproducing batch-to-batch consistency at industrial scale requires tight process control that is harder to achieve than with simpler dosage forms.
- Longer processing times: the multiple sequential steps involved add up to a longer overall production cycle compared with direct compression of conventional tablets.

V. TYPES OF MUPS

MUPS formulations are broadly classified by the final dosage form into which the pellets are incorporated — capsule-based or tablet-based — with the choice driven largely by drug properties, release requirements, and manufacturing feasibility.

A. Capsule-Based MUPS

Here, drug-loaded pellets — immediate-release, sustained-release, delayed-release, or enteric-coated as required — are simply filled into hard gelatin or HPMC capsule shells. On administration, the shell dissolves and releases the pellets to disperse through the gut.

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This route is attractive because pellets are never subjected to compressive force, so their coating stays intact and their release behaviour remains predictable; it also allows different pellet populations to be combined freely within a single capsule. Its principal drawbacks are somewhat higher packaging cost and marginally lower patient convenience relative to a tablet.

B. Tablet-Based MUPS

Tablet-based MUPS are produced by compressing coated (or uncoated) pellets, together with cushioning excipients, directly into a tablet. On administration, the tablet disintegrates and releases the individual pellets, each of which then behaves according to its own release design.

Tablets are generally easier to handle, package, transport, and swallow than capsules, and tend to cost less to manufacture and package. The trade-off is formulation difficulty: compression force can crack pellet coatings or deform the pellets outright, so careful excipient selection and compression-parameter optimization are needed to preserve pellet integrity and the intended release profile.

VI. COMPONENTS USED IN MUPS FORMULATION

Building a MUPS formulation draws on a specific set of pharmaceutical ingredients, each contributing to pellet formation, release control, coating performance, or overall stability.

A. Drug (Active Pharmaceutical Ingredient)

The physicochemical profile of the active — its solubility, stability, particle size, flow behaviour, and compatibility with the chosen excipients — largely dictates how it can be processed into pellets and how it will ultimately be released. MUPS technology is generally reserved for actives that call for sustained, delayed, enteric, or site-specific release, with the drug incorporated via extrusion-spheronization, layering, or another pelletization route depending on formulation needs.

B. Polymers

Polymers are central to controlling release rate and maintaining formulation stability. Hydrophilic or hydrophobic grades are selected according to the target release profile: sustained-release polymers extend drug liberation over time, while enteric grades shield acid-labile drugs from gastric degradation and release them only in the intestine. Hydroxypropyl methylcellulose (HPMC), ethyl cellulose, Eudragit grades, polyvinylpyrrolidone (PVP), and carbopol are among the polymers most commonly employed, with the specific choice driven by the drug's properties and the therapeutic objective.

C. Binders

Binders impart cohesiveness to the powder mass during pellet formation, promoting inter-particle adhesion and mechanical strength while maintaining the plasticity needed for wet massing and extrusion. PVP, starch paste, HPMC, and polyethylene glycol (PEG) are typical choices; binder level must be optimized carefully, since excess binder can yield overly hard pellets and distort the release profile.

D. Spheronizing Agents

Spheronizing agents lend the wet mass the plasticity and cohesiveness needed to form smooth, mechanically sound spherical pellets during the spheronization step. Microcrystalline cellulose (MCC) is the agent of choice by a wide margin, owing to its strong water-retention and binding characteristics, and is sometimes supplemented with starch or lactose depending on the formulation.

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E. Coating Materials

Coatings are applied to modify release behaviour, shield the drug from environmental stress, mask taste, and enhance stability. Enteric polymers (such as cellulose acetate phthalate, HPMC phthalate, or Eudragit L/S grades) block release in the stomach's acidic environment and permit it only in the intestine; sustained-release coatings (such as ethyl cellulose or Eudragit RS/RL) instead prolong release over an extended period. Coating thickness and uniformity are critical control points for achieving the intended release behaviour.

VII. PELLETIZATION TECHNIQUES USED IN MUPS

Pelletization converts powders or granules into small, free-flowing spherical units. The technique chosen depends on the drug's physicochemical properties, the target release profile, and practical manufacturing constraints; extrusion-spheronization, solution/suspension layering, powder layering, and hot-melt extrusion are the four routes most often used industrially.

A. Extrusion-Spheronization

The most widely used and industrially validated pelletization route. Drug and excipients are wet-massed with a granulating fluid, extruded into cylindrical strands of uniform diameter, and then transferred to a spheronizer, where frictional and rotational forces break the strands into segments that round off into spherical pellets.

The resulting pellets typically show excellent flow, a narrow size distribution, and good mechanical strength, with microcrystalline cellulose serving as the usual spheronizing aid. The method's reproducibility and scalability make it the preferred choice for sustained-release and enteric-coated pellet formulations.

B. Solution/Suspension Layering

A drug solution or suspension is sprayed onto inert starter cores (nonpareil seeds) in equipment such as a fluidized-bed processor; as the solvent evaporates, a drug layer builds up on the core surface, with repeated spraying cycles growing the pellet to the desired size.

This route offers precise control over drug loading and pellet size, making it well suited to low-dose actives and to formulations needing tightly controlled release, though the process can be time-consuming and demands careful control of spray and drying parameters.

C. Powder Layering

Dry drug powder is deposited onto starter cores wetted with a binder solution, with alternating cycles of binder spraying and powder application building the pellet up layer by layer.

The method suits high-drug-load formulations and actives that are sensitive to solvents or heat, since it avoids dissolving the drug in a liquid vehicle, though achieving a smooth, uniform layer can require careful process control.

D. Hot-Melt Extrusion

Drug is blended with a thermoplastic polymer and heated above its melting point to form a homogeneous molten mass, which is then forced through an extruder and subsequently shaped into pellets or granules.

Because no solvent is involved, the process is comparatively fast and environmentally favourable, and it is particularly effective at improving the solubility and bioavailability of poorly water-soluble drugs. Its main limitation is unsuitability for heat-labile actives, since the elevated processing temperatures can degrade thermally sensitive drugs.

VIII. EVALUATION PARAMETERS OF PELLETS

Rigorous evaluation is essential to confirm that a pellet batch meets the quality, mechanical strength, and release-performance standards required of the finished dosage form.

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A. Particle Size

Particle size governs coating uniformity, flow, capsule-filling behaviour, compressibility, and the ultimate release profile; sieve analysis, microscopy, and laser diffraction are the standard measurement techniques. Pharmaceutical pellets typically fall between 0.5 mm and 1.5 mm, and a narrow size distribution is preferred because it keeps coating thickness — and therefore release behaviour — consistent across the batch.

B. Friability

Friability testing gauges how well pellets resist abrasion and breakage during handling, transport, coating, and compression. A friabilator subjects pellets to controlled rotational stress for a set duration, and the resulting percentage weight loss is used as the friability index; lower values indicate stronger, more robust pellets.

C. Flow Properties

Good flow is essential for consistent capsule filling, coating, and compression. Particle size, shape, surface texture, and density all influence flow behaviour — spherical pellets flow especially well owing to reduced interparticle friction — and are typically assessed via angle of repose, bulk and tapped density, Carr's index, and Hausner ratio.

D. Drug Content

Drug-content analysis confirms that the active is distributed uniformly across the pellet batch and present at the intended concentration, typically by dissolving a representative sample and quantifying it spectrophotometrically or chromatographically. Uniform results indicate that mixing and pelletization were carried out correctly.

E. Dissolution Study

Dissolution testing, carried out with pharmacopoeial apparatus and media, characterizes the rate and extent of drug release under controlled conditions and is used to confirm whether a batch behaves as immediate-, sustained-, delayed-, or enteric-release. It remains one of the most important tools for formulation optimization, quality control, and predicting in-vivo performance.

IX. COATING OF PELLETS

Coating modifies release behaviour, shields the active from environmental stress, improves stability, and can mask unpleasant taste. Enteric and sustained-release coatings are the two approaches most commonly applied to pharmaceutical pellets.

A. Enteric Coating

Enteric coatings are designed to remain intact in the acidic environment of the stomach and dissolve only once the pellet reaches the higher pH of the intestine — a property useful for acid-labile drugs or actives that irritate the stomach lining. Cellulose acetate phthalate, HPMC phthalate, Eudragit L100, and Eudragit S100 are common enteric polymers, chosen for their pH-dependent solubility.

Fluidized-bed coaters are the equipment of choice for applying enteric coatings, since they deliver uniform coating thickness together with efficient drying; spray rate, inlet temperature, and target coating thickness all require careful optimization to achieve the desired release behaviour without compromising pellet integrity.

B. Sustained-Release Coating

Sustained-release coatings extend drug liberation over a prolonged interval, maintaining therapeutic concentrations for longer and cutting dosing frequency. Hydrophobic or semi-permeable polymers — ethyl cellulose, Eudragit RS, Eudragit RL, and polyvinyl acetate among them — form a barrier around the pellet that governs how quickly dissolution medium can penetrate and drug can diffuse out.

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This approach particularly benefits drugs with a short half-life or those requiring prolonged action, though coating thickness and uniformity must be tightly controlled, since even modest variation can shift the release profile.

X. DRUG RELEASE MECHANISMS IN MUPS

How drug is liberated from a MUPS pellet after administration depends on the pellet's internal composition, the polymer system used, coating thickness, drug solubility, and the pH environment it encounters along the gut — factors that formulators manipulate deliberately to achieve controlled, sustained, delayed, or site-specific release.

After the capsule shell or tablet disintegrates, the released pellets disperse through the stomach and intestine, presenting a comparatively large surface area for absorption. From that point, release typically proceeds through one or a combination of diffusion, dissolution, erosion, and osmotic mechanisms.

Diffusion-controlled release is the most frequently observed mechanism in coated pellets: dissolution medium penetrates the coating, dissolves the drug within, and the dissolved drug then diffuses back out through the membrane, at a rate set mainly by the coating's permeability and thickness.

Dissolution-controlled release occurs when the coating or matrix material itself gradually dissolves in gastrointestinal fluid; hydrophilic polymers typically hydrate and form a gel layer around the pellet through which drug slowly escapes, with the polymer's own dissolution rate governing the overall release profile.

Erosion-controlled release involves gradual physical erosion of the coating or matrix on contact with GI fluid, liberating entrapped drug as the barrier wears away — a pattern typical of biodegradable or swellable polymer systems.

In enteric-coated pellets, release is governed by pH-responsive polymers that stay intact in acidic gastric fluid but dissolve once the pellet reaches the intestine's more alkaline environment, producing a deliberately delayed release useful for protecting acid-sensitive drugs and limiting gastric irritation.

Sustained-release pellets rely on hydrophobic or semi-permeable polymer coatings to slow drug release over an extended window, stabilizing plasma concentrations and reducing dosing frequency; some formulations pair immediate-release pellets with sustained-release ones in the same dosage unit to combine a rapid onset with prolonged therapeutic action.

Formulation variables — pellet size, surface area, polymer choice, coating thickness, and porosity — all interact to determine the final release profile, making careful optimization of these parameters essential to achieving a formulation's intended performance.

XI. APPLICATIONS OF MUPS

The flexibility of MUPS technology has led to its adoption across several therapeutic release strategies.

A. Sustained Release

Pellets engineered for gradual, extended drug liberation maintain therapeutic concentrations over a longer window, reducing dosing frequency and smoothing out the plasma-concentration profile — typically achieved with hydrophobic or semi-permeable polymers such as ethyl cellulose and Eudragit grades.

B. Delayed Release

Enteric-coated MUPS pellets withhold release until the intestine is reached, protecting acid-labile drugs and reducing gastric irritation — useful wherever intestinal absorption or site-specific delivery within the gut is the goal.

C. Chronotherapy

Because MUPS pellets allow precise control over lag time before release begins, they are well suited to chronotherapeutic dosing, where drug is timed to coincide with a disease's circadian symptom pattern — relevant to conditions such as asthma, hypertension, arthritis, and peptic ulcer disease.

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D. Combination Therapy

Pellet populations with different release profiles, or even different actives, can be combined in one capsule or tablet, enabling combination products and keeping otherwise incompatible drugs physically separated within their own pellets — an approach commonly used in managing chronic conditions requiring multiple medications.

XII. MARKETED PREPARATIONS OF MUPS

MUPS technology is now well established commercially, with several proton-pump-inhibitor products among its best-known applications. Omeprazole MUPS tablets, marketed by AstraZeneca as Losec MUPS, compress enteric-coated omeprazole pellets into a single tablet, protecting the acid-labile drug in the stomach while allowing release in the intestine.

Esomeprazole magnesium delayed-release pellets, sold by AstraZeneca as Nexium, use the same enteric-coated pellet principle to achieve delayed release and reliable acid suppression. Lansoprazole delayed-release capsules, marketed by Takeda Pharmaceutical Company as Prevacid, similarly rely on enteric-coated pellets designed for intestinal release, and pantoprazole sodium delayed-release pellet products from several manufacturers follow the same approach to protect proton-pump inhibitors from acidic degradation.

Beyond gastric-acid-suppressant products, MUPS technology also underpins combination and sustained-release formulations that pair immediate- and sustained-release pellets to achieve rapid onset followed by prolonged action, including select antibiotic, cardiovascular, and gastrointestinal products. Multinational manufacturers including AstraZeneca, Takeda Pharmaceutical Company, Abbott Laboratories, and Sun Pharmaceutical Industries maintain pellet-based formulations in their portfolios, and continuing advances in coating and pelletization technology are likely to expand this list further.

XIII. RECENT ADVANCES IN MUPS

Continuing research has pushed MUPS technology in several directions simultaneously. Newer functional polymers — Eudragit derivatives, polyvinyl acetate, and various biodegradable grades — offer tighter control over release kinetics and better coating uniformity than earlier materials.

Nanotechnology integration is a notable recent trend: incorporating nanoparticles, nanosuspensions, or lipid-based carriers into pellets has improved the solubility and bioavailability of drugs that dissolve poorly on their own.

Hot-melt extrusion has gained ground as a solvent-free pelletization route that also shortens processing time, and is increasingly used both to boost the solubility of poorly soluble drugs and to support continuous-manufacturing workflows at industrial scale.

Coating technology has likewise advanced, with modern fluidized-bed systems delivering more uniform, defect-free coatings and enabling new chronotherapeutic coating designs timed to biological rhythms. Compression-resistant pellet designs, aided by specialized cushioning agents, are helping tablet-based MUPS formulations survive compression without coating damage.

Quality by Design (QbD) and Process Analytical Technology (PAT) frameworks are being applied increasingly to MUPS manufacturing, helping identify critical process variables and tighten batch-to-batch reproducibility. Targeted and colon-specific coatings are also being developed, with particular relevance to inflammatory bowel disease, colon cancer, and other localized gastrointestinal conditions.

XIV. CHALLENGES IN MUPS FORMULATION AND MANUFACTURING

Despite its advantages, MUPS formulation and manufacturing still present a range of technical obstacles that formulators must actively manage.

Maintaining consistent pellet size and shape is a persistent challenge, since dimensional variation feeds directly into coating thickness, release profile, flow, and content uniformity — all of which demand tight control of formulation and process parameters during pelletization.

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Coating uniformity is equally critical in modified-release products, where uneven thickness can translate into variable release, dose dumping, or reduced efficacy; achieving reproducible coating quality requires careful optimization of spray rate, atomization pressure, inlet temperature, and drying conditions.

For tablet-based formulations, compression itself is a risk point — pellets can fracture, deform, or suffer coating rupture under compressive force, altering the intended release profile unless suitable cushioning agents and compression settings are used to protect pellet integrity.

Drug-excipient compatibility is another concern, since certain actives can interact with polymers, binders, or coating agents to cause instability or degradation; moisture- and heat-sensitive drugs are particularly exposed, given that both pelletization and coating processes can involve heat and moisture.

Scale-up introduces its own difficulties, since minor shifts in process conditions during large-scale manufacture can affect pellet quality and release behaviour, and specialized equipment together with skilled operators is usually required, adding to cost and complexity. Segregation of pellets by size or density during mixing, filling, or compression can further cause dose variation and content-uniformity problems, and storage stability remains a concern, since temperature and humidity exposure can compromise coating integrity and drug stability over time.

Notwithstanding these obstacles, ongoing improvements in pelletization technique, coating technology, and process optimization continue to raise the reliability and consistency of MUPS products reaching the market.

XV. FUTURE PROSPECTS OF MUPS

Several converging trends point toward continued growth of MUPS as a drug-delivery platform. Advanced polymer chemistry is expected to enable ever more precise, programmable release profiles tailored to specific therapeutic needs.

The rise of personalized medicine also plays to MUPS's strengths: because pellet populations with different drug loads or release characteristics can be combined flexibly, formulations can in principle be tailored to a patient's age, disease state, or individual requirements.

Continuous manufacturing and automation are likely to improve industrial-scale production of pellet-based formulations, with technologies such as hot-melt extrusion, 3D printing, and Quality-by-Design process frameworks expected to raise reproducibility while lowering cost.

Chronotherapeutic applications also represent a significant growth area, since MUPS is well positioned to deliver drugs timed to a patient's biological rhythm — relevant to circadian-pattern conditions such as asthma, arthritis, hypertension, and gastric disorders.

As demand grows for controlled-release, patient-friendly oral therapies, pharmaceutical manufacturers are likely to continue investing in pelletization and coating technology, positioning MUPS as an increasingly central platform in modified-release oral drug delivery.

XVI. CONCLUSION

Multiple Unit Pellet System technology has matured into one of the more dependable strategies available for modified-release oral drug delivery, offering more even drug distribution, a materially lower dose-dumping risk, less gastric irritation, and better patient compliance than conventional single-unit dosage forms.

Its success rests on a well-developed set of pelletization routes — extrusion-spheronization, solution and powder layering, and hot-melt extrusion — paired with careful selection of polymers, binders, spheronizing agents, and coating materials, and validated through evaluation parameters such as particle size, friability, flow, drug content, and dissolution behaviour.

MUPS already underpins a range of commercial products spanning sustained release, enteric-coated formulations, chronotherapy, and combination therapy, and continues to benefit from advances in polymer science, coating technology, nanotechnology integration, and continuous manufacturing.

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Manufacturing and formulation challenges remain, but sustained research investment and process innovation are steadily narrowing them, and the growing demand for patient-friendly, targeted, modified-release therapy suggests that MUPS will remain an important and expanding platform in oral drug delivery for years to come.

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