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Review On Repurposing Of Old Drugs For New Indications Focus: Aspirin, Metformin, Hydroxychloroquine

[1]Siddhi Zodge, [2]Omkar Gore, [3] Vijaykumar kale ,[4] Mahesh Thakare , [5] Vaibhav Narwade,[6]Riddhi Zodge

[1]Student, Kasturi Shikshan Sanstan College of Pharmacy, Shikrapur, Pune

[2]Assistant Professor, Kasturi Shikshan Sanstan College of Pharmacy, Shikrapur, Pune

[3]Principle, Kasturi Shikshan Sanstan College of Pharmacy, Shikrapur, Pune

[4] Head of Department, Kasturi Shikshan Sanstan College of Pharmacy, Shikrapur, Pune

[5]Assistant Professor, Kasturi Shikshan Sanstan College of Pharmacy, Shikrapur, Pune

[6]Student, KJ Trinity college of pharmacy,Pune

[1]Department of Pharmacy

[1]Kasturi Shikshan Sanstan College of Pharmacy, Shikrapur, Pune

Abstract

Drug repurposing, also known as drug repositioning, is an innovative and cost-effective strategy that involves identifying new therapeutic uses for existing drugs beyond their original medical indications. This approach has gained significant attention due to rising drug development costs, lengthy regulatory processes, and increasing global disease burden. Repurposed drugs benefit from established safety profiles, known pharmacokinetics, and reduced risk of failure compared to novel drug discovery. Among several repurposed agents, aspirin, metformin, and hydroxychloroquine have emerged as prominent examples with expanding therapeutic applications. Aspirin, traditionally used as an analgesic and antiplatelet agent, has demonstrated potential anticancer, anti-inflammatory, and neuroprotective effects. Metformin, primarily an antidiabetic drug, has shown promising roles in oncology, cardiovascular diseases, and metabolic disorders. Hydroxychloroquine, originally developed as an antimalarial agent, has been widely explored for autoimmune and inflammatory conditions. This review highlights the concept of drug repurposing, mechanisms involved, and recent advances in repurposing aspirin, metformin, and hydroxychloroquine for new clinical indications, along with challenges and future perspectives.

Keywords

Drug repurposing; Aspirin; Metformin; Hydroxychloroquine; New indications; Pharmacological management

1.INTRODUCTION

Drug discovery and development is a complex, time-consuming, and costly process that often spans more than a decade before a new therapeutic agent reaches clinical use. Despite major advances in pharmaceutical sciences, the success rate of newly developed drugs remains relatively low due to safety concerns, lack of efficacy, and high attrition during clinical trials. In this context, **drug repurposing**, also known as drug repositioning, has emerged as an effective and innovative strategy to identify new therapeutic indications for existing drugs with well-established safety profiles. (1)

Drug repurposing involves the investigation of approved or previously developed drugs for diseases other than those for which they were originally indicated. Since repurposed drugs have already undergone extensive preclinical and clinical evaluation, this approach significantly reduces development time, cost, and risk when compared to traditional drug discovery pathways. Repurposing also offers a rapid response to emerging medical needs and unmet therapeutic challenges, making it particularly valuable in areas such as oncology, infectious diseases, neurological disorders, and chronic inflammatory conditions. (2)

Several classical drugs have demonstrated unexpected pharmacological effects beyond their original therapeutic use. Among them, **aspirin, metformin, and hydroxychloroquine** represent prominent examples of old drugs with diverse and expanding clinical applications. These drugs have been in medical use for several decades and possess well-characterized pharmacokinetic and pharmacodynamic properties, making them ideal candidates for repurposing research. (3)

Aspirin (acetylsalicylic acid) was initially introduced as an analgesic, antipyretic, and anti-inflammatory agent. Over time, its antiplatelet activity led to widespread use in the prevention of cardiovascular diseases. Recent studies have further expanded its therapeutic potential, revealing roles in cancer prevention, neuroprotection, and modulation of inflammatory and immune pathways. (4)

Metformin, a first-line oral antidiabetic agent used primarily in the management of type 2 diabetes mellitus, has gained significant attention for its pleiotropic effects. Beyond glycemic control, metformin has shown promising benefits in cancer prevention, cardiovascular protection, metabolic disorders, neurodegenerative diseases, and aging-related conditions. Its ability to modulate cellular metabolism and signaling pathways such as AMP-activated protein kinase (AMPK) underlies its broad therapeutic potential. (5)

Hydroxychloroquine, originally developed as an antimalarial drug, has been widely used in the treatment of autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. Its immunomodulatory and anti-inflammatory properties have led to investigations into its role in viral infections, inflammatory disorders, and cancer therapy, particularly through the inhibition of autophagy and immune signaling pathways. (6)

This review aims to provide a comprehensive overview of the concept of drug repurposing with a focused discussion on aspirin, metformin, and hydroxychloroquine. It highlights their mechanisms of action, emerging therapeutic applications, clinical evidence, and future prospects. Understanding the repurposing potential of these well-established drugs may contribute to the development of effective, affordable, and safer therapeutic strategies for a wide range of diseases. (7)

2. Concept of Drug Repurposing

Drug repurposing, also referred to as drug repositioning or drug reprofiling, is the process of identifying new therapeutic indications for existing drugs that are already approved, previously tested, or shelved during drug development. Unlike conventional drug discovery, which begins with target identification and lead optimization, drug repurposing capitalizes on prior knowledge of a drug's pharmacological properties, safety profile, bioavailability, and toxicity. This strategy has gained increasing importance in modern pharmaceutical research as it offers a faster, safer, and more economical pathway for drug development (8)

Drug repurposing involves:

- Identifying new disease targets for existing drugs
- Understanding alternative mechanisms of action
- Utilizing computational, experimental, and clinical approaches

Advantages of Drug Repurposing

1. **Reduced Development Times**

Drug repurposing significantly shortens the time required to bring a therapy to clinical use, as repurposed drugs have already undergone extensive preclinical and clinical testing for their original indications.

2. **Lower Research and Development Costs**
Since safety, toxicity, and pharmacokinetic data are already available, the overall cost of drug development is

3. substantially reduced compared to de novo drug discovery.

4. **Established Safety Profiles**
Repurposed drugs such as aspirin, metformin, and hydroxychloroquine have decades of clinical use, providing well-documented safety, dosing, and adverse effect profiles.

5. **Higher Success Rate**
The likelihood of clinical success is higher in drug repurposing because many uncertainties related to drug absorption, metabolism, and toxicity have already been addressed.

6. **Faster Regulatory Approval**
Regulatory pathways for repurposed drugs are often simplified, enabling quicker approval

Disadvantages of Drug Repurposing

1. **Limited Patent Protection**
Most old drugs such as aspirin, metformin, and hydroxychloroquine are off-patent, which reduces commercial incentives for pharmaceutical companies to invest in costly clinical trials for new indications.

2. **Regulatory Challenges**
Even though the drugs are already approved, obtaining regulatory approval for new indications still requires extensive clinical evidence, which can be time-consuming and resource-intensive.

3. **Dose Optimization Issues**
The optimal dose for a new indication may differ significantly from the original use, increasing the risk of suboptimal efficacy or unexpected adverse effects.

4. **Safety Concerns in New Populations**
Repurposed drugs may exhibit different safety profiles when used in new patient populations, such as pediatric, geriatric, or immunocompromised patients.

5. **Off-Target and Long-Term Effects**
Drugs repurposed for chronic or high-dose use may lead to unforeseen off-target effects or cumulative toxicity over long treatment durations.

6. **Limited Clinical Evidence**
Many repurposed indications are initially supported by observational or preclinical studies, which may not always translate into robust clinical effectiveness.

3. Aspirin: From Analgesic to Multidimensional Therapeutic Agent

Aspirin is one of the oldest and most extensively studied drugs in medical history. Originally introduced in the late nineteenth century as an analgesic, antipyretic, and anti-inflammatory agent, aspirin has since evolved into a multidimensional therapeutic drug with applications extending far beyond pain and fever management. Its long-standing clinical use, low cost, and well-established safety profile make aspirin a prime example of successful drug repurposing. (9)

3.1 Original Indications

Aspirin (acetylsalicylic acid) was initially developed as an analgesic, antipyretic, and anti-inflammatory drug. It is widely used for pain relief and prevention of cardiovascular events due to its antiplatelet activity. (10)

3.2 Repurposed Indications

Aspirin, originally introduced as an analgesic and antipyretic agent, has been extensively repurposed for a wide range of therapeutic indications due to its well-established pharmacological properties. One of its most important repurposed uses is in the prevention of cardiovascular diseases, where low-dose aspirin acts as an antiplatelet agent by irreversibly inhibiting cyclooxygenase-1 and reducing thromboxane A_2–mediated platelet aggregation. In addition, long-term aspirin use has been associated with a reduced risk of several cancers, particularly colorectal cancer, through mechanisms involving inhibition of inflammation, induction of apoptosis, and suppression of tumor growth. Aspirin has also demonstrated neuroprotective potential in neurodegenerative disorders by decreasing neuroinflammation and oxidative stress. Furthermore, it is used in the prevention of preeclampsia in high-risk pregnancies and is being explored as an adjunct therapy in infectious, inflammatory, and metabolic disorders. These diverse applications highlight aspirin's successful transition from a simple analgesic to a multidimensional therapeutic agent through drug repurposing. (11)

3.2.1 Cancer Prevention and Therapy

Aspirin has demonstrated chemopreventive effects, particularly in colorectal, breast, and prostate cancers. Its anticancer activity is attributed to cyclooxygenase (COX) inhibition, reduction of inflammation, and modulation of platelet-mediated tumor growth. (12)

3.2.2 Neurodegenerative Disorders

Low-dose aspirin has been investigated for its potential neuroprotective effects in conditions such as Alzheimer's disease by reducing neuroinflammation and oxidative stress. (13)

3.2.3 Anti-inflammatory and Immunomodulatory Effects

Aspirin plays a role in modulating immune responses and has been studied in chronic inflammatory conditions. (14)

4. Metformin: Beyond Glycemic Control

4.1 Original Indications

Metformin is a first-line oral antidiabetic drug used in the management of type 2 diabetes mellitus. It improves insulin sensitivity and reduces hepatic glucose production. (15)

4.2 Repurposed Indications

4.2.1 Oncology

Metformin has shown promising anticancer properties by activating AMP-activated protein kinase (AMPK), inhibiting mTOR signaling, and reducing cancer cell proliferation. It has been studied in breast, lung, colorectal, and prostate cancers. (16)

4.2.2 Cardiovascular Diseases

Metformin reduces cardiovascular risk factors by improving lipid profiles, reducing inflammation, and enhancing endothelial function. (17)

4.2.3 Polycystic Ovary Syndrome (PCOS)

Metformin is widely repurposed for managing insulin resistance and hormonal imbalance in PCOS.

5. Hydroxychloroquine: An Immunomodulatory Agent

5.1 Original Indications

Hydroxychloroquine was originally developed as an antimalarial drug.

5.2 Repurposed Indications

Hydroxychloroquine has also been investigated for its antiviral potential, as it can increase endosomal pH and interfere with viral entry and replication, leading to its evaluation in various viral infections. In oncology, hydroxychloroquine is being explored as an adjuvant therapy due to its ability to inhibit autophagy, a survival mechanism exploited by cancer cells, thereby enhancing the efficacy of chemotherapy and radiotherapy. Additionally, its role in managing chronic inflammatory conditions and metabolic complications associated with immune dysregulation is under investigation. These repurposed indications highlight hydroxychloroquine's transition from a conventional antimalarial drug to a versatile therapeutic agent in modern medicine. (18)

5.2.1 Autoimmune Diseases

Hydroxychloroquine is extensively used in rheumatoid arthritis and systemic lupus erythematosus due to its immunomodulatory and anti-inflammatory effects. (18)

5.2.2 Antiviral and Anti-inflammatory Applications

Hydroxychloroquine has been explored for viral infections and inflammatory conditions due to its ability to alter endosomal pH and inhibit immune activation. (19)

5.2.3 Dermatological Disorders

It is used in conditions such as photosensitive dermatoses and chronic cutaneous lupus.

6. Epidemiology

6.1 **Global burden relevant to repurposing opportunities (overview)**

• Many repurposing opportunities arise from large, growing disease burdens — e.g., chronic noncommunicable diseases (diabetes, cardiovascular disease, cancer, autoimmune disorders) — which create demand for affordable, safe therapies that can be redeployed. (See 1.2–1.4 for drug-specific prevalence.) (20)

6.2 **Aspirin — population use & cardiovascular context**

• Aspirin remains widely used for secondary prevention but inappropriate for many in primary prevention; national surveys (2013–2020) show substantial aspirin use for primary prevention in higher-income countries despite updated guidance limiting such use. (21)

6.3 **Metformin — diabetes and wider population at risk**

• Type 2 diabetes prevalence is large and rising globally (WHO estimates: roughly double-digit percent adult prevalence increases over recent decades), creating a large and growing user base for metformin and a large pool of patients in whom metformin's non-glycaemic benefits (oncology, aging, metabolic syndrome) are being investigated. (22)

6.4 **Hydroxychloroquine (HCQ) — autoimmune disease burden and usage**

• HCQ is widely used in autoimmune diseases (SLE, RA) and remains an established part of therapy in these populations; interest in antiviral/oncology uses spiked during COVID-19, but safety and efficacy debates altered prescribing patterns and regulatory guidance in some settings. Regional manufacturing concentrations (notably India) influence global supply. (23)

7. Market Trends (global & drug-level)

7.1 **Overall drug-repurposing market**

• The drug-repurposing market is already large and expanding — estimates place the global market at **~USD 32–33 billion in 2024**, with projected growth into the mid-2030s (CAGR ≈ 4–5% in many forecasts). This growth reflects rising investment in translational research, AI-driven repurposing platforms, and regulatory pathways (e.g., 505(b)(2)). (24)

7.2 **Aspirin market**

• The commercial aspirin drugs market (finished-product market) is modest compared with the overall repurposing market (valuations around **USD 1.3 billion in 2023** with steady low-single-digit CAGR projected), but aspirin's clinical importance for large population indications (CVD prevention, cancer prevention studies) makes it strategically important for repurposing research rather than big revenue growth. (25)

7.3 **Metformin market**

• Metformin as a product category remains large due to global diabetes prevalence; market reports estimate **multi-billion USD markets** for metformin HCl and sustained-release formulations with projected growth driven by rising diabetes prevalence and adoption of extended-release products. Interest in repurposed uses (oncology, aging) could broaden demand, especially for novel formulations. (26)

7.4 **Hydroxychloroquine market**

• HCQ market estimates vary (reports in the 2024–2025 period put total market value in the range of **~USD 0.9–4.2 billion** depending on scope), and forecasts show steady growth tied to autoimmune disease prevalence and expanded therapeutic applications or formulations. India's dominant manufacturing share is an important supply-chain factor. (27)

8. Key Market Drivers & Signals

• **Large target populations** (diabetes, CVD, cancer risk groups, autoimmune diseases) create high potential demand for proven, inexpensive drugs — favorable for repurposing.
• **Regulatory & pathway evolution** (e.g., 505(b)(2), adaptive trials, real-world evidence) shortens time-to-market for repurposed indications, increasing commercial attractiveness despite weak patents.
• **Technological enablers**: AI/ML, large-scale EHR mining, and systems biology accelerate candidate identification, driving venture and pharma interest (visible in market forecasts).
• **Public-health shocks** (e.g., COVID-19) temporarily altered demand and perception (notably for HCQ) — causing rapid expansion then retrenchment in certain markets and highlighting reputational/regulatory risk. (28)

9. Regional & Supply Considerations

• **Manufacturing concentration** (egIndia supplies a large share of global HCQ active pharmaceutical ingredient) affects pricing, availability, and strategic sourcing for repurposing programmes.

• **High-income vs low-income markets**: HICs drive R&D and premium formulation uptake (ER/novel formulations); LMICs depend on low-cost generics — repurposing that yields low-cost, high-impact interventions may have outsized public-health value in LMICs (29)

10. Challenges & Risks Affecting Market Uptake

• **Commercial incentives** are limited for off-patent drugs (weak IP), creating reliance on public funding, academic–industry partnerships, or new business models (data exclusivity, formulation patents).
• **Regulatory evidence requirements**: Even repurposed drugs need indication-specific trials for label expansion — generating cost/time barriers.
• **Safety perception & politicization**: High-profile controversies (e.g., HCQ during COVID-19) can damage market confidence or trigger regulatory warnings that slow adoption. (30)

11. Implications for Research & Industry (practical takeaways)

• Prioritize repurposing candidates with **large potential patient populations** (metformin in oncology/aging; aspirin in cancer prevention subsets) to maximize public-health impact• Leverage **novel formulations** (ER metformin, targeted HCQ delivery, enteric/coated aspirin) to create differentiable products and limited-term exclusivity.
• Use **real-world evidence** and pragmatic/adaptive trials to reduce trial cost and accelerate label expansion — attractive to payers and regulators. • Public-private partnerships and philanthropic funding remain important for trials where commercial ROI is limited but public-health benefit is high.(31)

12. Mechanisms Involved in Drug Repurposing

- Modulation of alternative molecular pathways
- Targeting inflammatory and immune signaling
- Metabolic reprogramming
- Epigenetic regulation

Understanding these mechanisms is crucial for successful clinical translation.

13. Challenges in Drug Repurposing

- Limited patent protection
- Regulatory and approval challenges
- Dose optimization for new indications
- Risk of off-target effects

Despite these limitations, strategic research and clinical trials can overcome these challenges.

14. Future Perspectives

The future of drug repurposing holds significant promise as advances in biomedical research, computational sciences, and clinical pharmacology continue to transform the landscape of therapeutic discovery. For well-established drugs such as aspirin, metformin, and hydroxychloroquine, ongoing and future research is expected to further expand their clinical applications by uncovering novel mechanisms of action and disease-specific benefits. The integration of genomics, proteomics, and metabolomics with large-scale clinical data will enable a more precise understanding of how these drugs interact with multiple molecular targets, thereby facilitating the identification of new indications based on disease biology rather than empirical observations alone. (32)

Emerging technologies such as artificial intelligence and machine learning are anticipated to play a pivotal role in accelerating drug repurposing efforts. These tools can analyze vast datasets from electronic health records, clinical trials, and molecular databases to predict new drug–disease associations with greater accuracy. For aspirin, future studies may focus on personalized dosing strategies to maximize its anticancer and cardioprotective benefits while minimizing adverse effects. In the case of metformin, ongoing trials exploring its role in cancer therapy, neurodegenerative diseases, and aging-related conditions are likely to provide stronger clinical evidence and refine its use beyond diabetes management. Hydroxychloroquine research may advance through better patient stratification and combination therapies, particularly in autoimmune diseases and cancer, ensuring improved efficacy and safety. (33)

Additionally, regulatory frameworks are expected to evolve to better accommodate drug repurposing, encouraging academic–industry collaborations and facilitating faster approval of new indications. Greater emphasis on real-world evidence and adaptive clinical trial designs may further support the validation of repurposed drugs. Overall, the continued exploration of aspirin, metformin, and hydroxychloroquine exemplifies the potential of drug repurposing to deliver cost-effective, accessible, and innovative therapeutic solutions, ultimately improving patient outcomes and addressing unmet medical needs across diverse disease areas. (34)

15.Formulation Development: Excipients and Bases

Formulation development is a critical component in the successful repurposing of old drugs for new therapeutic indications. Although drugs such as aspirin, metformin, and hydroxychloroquine are already available in established dosage forms, repurposing often necessitates modification of formulations to optimize drug delivery, improve patient compliance, enhance bioavailability, and reduce adverse effects for the new indication. Selection of appropriate excipients and formulation bases plays a key role in achieving these objectives. (35)

In the case of **aspirin**, formulation development focuses on minimizing gastrointestinal irritation while maintaining therapeutic efficacy, especially when repurposed for long-term use in cardiovascular or cancer prevention. Enteric-coated tablets, sustained-release formulations, and buffered preparations are commonly employed. Excipients such as cellulose derivatives, starches, and polymers like methacrylic acid copolymers are used as coating agents to prevent drug release in the stomach. Alkalizing agents and buffering bases are also incorporated to reduce gastric acidity and improve tolerability. (36)

For **metformin**, which is highly water-soluble and associated with gastrointestinal side effects, formulation strategies aim to enhance tolerability and control drug release. Extended-release and sustained-release formulations are widely developed using hydrophilic matrix systems. Excipients such as hydroxypropyl methylcellulose (HPMC), polyethylene glycol, lactose, and magnesium stearate are commonly used to regulate drug release, improve tablet integrity, and enhance patient

adherence, particularly when repurposed for chronic conditions such as cancer or metabolic disorders. (37)

Hydroxychloroquine formulation development often emphasizes dose accuracy, stability, and targeted delivery for autoimmune, antiviral, or anticancer applications. Conventional oral tablets typically contain excipients such as microcrystalline cellulose, starch, and binders to ensure uniform drug distribution and mechanical strength. For repurposed indications, novel formulations including nanoparticles, liposomal systems, and topical or injectable bases are being explored to improve tissue targeting and reduce systemic toxicity. Lipid-based excipients, surfactants, and biodegradable polymers are increasingly investigated to enhance therapeutic efficacy. (38)

Overall, formulation development and the careful selection of excipients and bases are essential in drug repurposing to adapt existing drugs to new therapeutic needs. Optimized formulations can improve safety, efficacy, and patient compliance, thereby enhancing the clinical success of repurposed drugs such as aspirin, metformin, and hydroxychloroquine. (39)

16.Standardization and Regulatory Aspects

Standardization and regulatory oversight play a crucial role in the successful implementation of drug repurposing strategies, particularly for well-established drugs such as aspirin, metformin, and hydroxychloroquine. Although these drugs are already approved for specific indications, their use for new therapeutic purposes requires rigorous standardization to ensure quality, safety, efficacy, and reproducibility in the new clinical context. Standardization involves maintaining consistent drug quality, purity, dosage forms, and bioavailability, as variations in formulation or dosing may significantly influence therapeutic outcomes when a drug is repurposed for a different indication.

From a regulatory perspective, repurposed drugs must undergo evaluation through established regulatory pathways to gain approval for new indications. Regulatory authorities such as the US Food and Drug Administration (FDA), European Medicines Agency (EMA), and national drug regulatory bodies require robust scientific and clinical evidence demonstrating efficacy and safety for the proposed new use. Depending on the extent of available data, repurposed drugs may follow abbreviated regulatory pathways, such as the FDA's 505(b)(2) pathway, which allows reliance on existing data while requiring additional studies specific to the new indication. However, dose optimization, duration of therapy, and potential drug–drug interactions must be reassessed for the repurposed use.

Clinical trials remain a key regulatory requirement, even for old drugs, to confirm therapeutic benefit and identify indication-specific risks. For drugs like aspirin, metformin, and hydroxychloroquine, post-marketing surveillance and pharmacovigilance are particularly important, as long-term or off-label use may reveal rare adverse effects or safety concerns in new patient populations. Ethical considerations, including informed consent and rational off-label prescribing, are also integral to regulatory compliance.

In addition, intellectual property and patent challenges can influence the commercial development of repurposed drugs, as many old drugs are off-patent. Regulatory incentives, data exclusivity, and public–private partnerships may help overcome these barriers. Overall, effective standardization and well-defined regulatory frameworks are essential to ensure that repurposed drugs are safely and responsibly integrated into clinical practice, maximizing their therapeutic potential while protecting patient safety. (40)

17.Diversity

Drug repurposing exhibits remarkable **diversity** in terms of therapeutic areas, mechanisms of action, patient populations, and formulation strategies. The repurposing of aspirin, metformin, and hydroxychloroquine clearly demonstrates how a single drug can address multiple diseases through different biological pathways. (41)

17.1. Therapeutic Diversity

Repurposed drugs are applied across a wide range of disease conditions beyond their original indications.

- **Aspirin**: Cardiovascular diseases, cancer prevention, neurodegenerative disorders, pregnancy-related complications, and chronic inflammatory conditions.
- **Metformin**: Oncology, cardiovascular diseases, polycystic ovary syndrome (PCOS), neurodegenerative disorders, metabolic syndrome, and aging-related diseases.
- **Hydroxychloroquine**: Autoimmune diseases, dermatological disorders, viral infections, inflammatory conditions, and adjunct cancer therapy.

This therapeutic diversity highlights the versatility of old drugs in addressing multiple unmet medical needs.

17.2. Mechanistic Diversity

Repurposing is driven by the ability of drugs to act through **multiple molecular and cellular pathways**.

- **Aspirin**: Cyclooxygenase (COX) inhibition, antiplatelet action, anti-inflammatory signaling, immune modulation, and apoptosis induction in cancer cells.
- **Metformin**: Activation of AMP-activated protein kinase (AMPK), inhibition of mTOR signaling, metabolic reprogramming, reduction of insulin resistance, and anti-inflammatory effects.
- **Hydroxychloroquine**: Inhibition of lysosomal activity, alteration of endosomal pH, suppression of immune activation, and inhibition of autophagy.

This mechanistic diversity allows a single drug to exert beneficial effects in different pathological conditions.

17.3. Clinical Diversity

Repurposed drugs are used in diverse **clinical settings and patient populations**.

- Preventive therapy (aspirin in cardiovascular disease and cancer prevention)
- Chronic disease management (metformin in metabolic and endocrine disorders)
- Autoimmune and inflammatory disease control (hydroxychloroquine in rheumatoid arthritis and lupus)
- Adjunct therapy (metformin and hydroxychloroquine in cancer treatment)

17.4. Population Diversity

Repurposed drugs are applicable across varied demographic groups:

- Adults and elderly populations (aspirin for cardiovascular protection)
- Women-specific conditions (metformin in PCOS, aspirin in preeclampsia prevention)
- Immunocompromised patients (hydroxychloroquine in autoimmune disorders)

However, careful dose adjustment and safety monitoring are essential.

17.5. Formulation and Delivery Diversity

Drug repurposing often requires diverse formulation approaches:

- **Aspirin**: Enteric-coated, sustained-release, and buffered formulations
- **Metformin**: Immediate-release, extended-release, and combination formulations
- **Hydroxychloroquine**: Oral tablets, topical formulations, and emerging nanoformulations

These variations improve efficacy, safety, and patient compliance for new indications.

17.6. Research and Evidence Diversity

Evidence supporting drug repurposing originates from multiple sources:

- Epidemiological and observational studies
- Preclinical laboratory research
- Clinical trials and real-world data
- Computational and bioinformatics analyses

This diversity strengthens the scientific foundation of repurposing strategies.

17.7. Regulatory and Developmental Diversity

Repurposed drugs follow different regulatory pathways depending on the indication, dose, and formulation, ranging from off-label use to formal regulatory approval for new indications.

17.8. Economic and Global Health Diversity

Repurposed drugs are low-cost and widely accessible, making them especially valuable in:

- Low- and middle-income countries
- Resource-limited healthcare systems
- Global public health initiatives

18. Conclusion

Drug repurposing represents a strategic and innovative approach in pharmaceutical research, aimed at identifying new therapeutic applications for existing drugs with well-established safety and pharmacological profiles. In an era where conventional drug discovery is increasingly challenged by high costs, prolonged development timelines, and high failure rates, repurposing offers a practical solution to accelerate the availability of effective treatments. By utilizing prior clinical and preclinical knowledge, this approach minimizes risk while maximizing the therapeutic potential of known drugs.

The present review highlights the significance of drug repurposing through the examples of **aspirin, metformin, and hydroxychloroquine**, three widely used and well-characterized drugs that have successfully transcended their original indications. Aspirin, initially introduced as an analgesic and antipyretic agent, has evolved into a cornerstone therapy for cardiovascular disease prevention due to its antiplatelet effects. In addition, accumulating evidence supports its role in cancer prevention, particularly colorectal cancer, as well as in neuroprotection and inflammatory modulation. These expanded applications underscore aspirin's multifaceted mechanism of action and its relevance in long-term disease management.

Metformin, a first-line oral antidiabetic drug, has gained substantial attention beyond glucose control. Its ability to regulate cellular metabolism, activate AMP-activated protein kinase (AMPK), and reduce systemic inflammation has positioned it as a promising candidate for repurposing in oncology, cardiovascular diseases, neurodegenerative disorders, and aging-related conditions. Numerous observational and experimental studies suggest that metformin may reduce cancer incidence and improve overall survival, highlighting its potential as a disease-modifying agent.

Hydroxychloroquine, originally developed as an antimalarial drug, has become an essential therapeutic option in autoimmune and inflammatory diseases such as rheumatoid arthritis and systemic lupus erythematosus. Its immunomodulatory properties have prompted investigations into its antiviral and anticancer potential, particularly through inhibition of immune activation and autophagy pathways. Although its use in certain emerging indications remains controversial and requires further clinical validation, hydroxychloroquine continues to illustrate the adaptability of old drugs in addressing new therapeutic challenges.

In conclusion, the repurposing of aspirin, metformin, and hydroxychloroquine demonstrates the immense value of revisiting established drugs to uncover novel clinical benefits. Continued advancements in molecular biology, computational drug screening, and clinical research are expected to further enhance the identification and validation of repurposed drug candidates. Drug repurposing not only reduces development costs and timelines but also contributes to affordable and accessible healthcare solutions. Therefore, it remains a vital strategy for addressing unmet medical needs and improving global health outcomes.

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