ACTIVE CONSTITUENTS OF OSTOMY DEJECTA AND THEIR IMPACT ON PERISTOMAL SKIN HEALTH IN EXPERIMENTAL MODELS

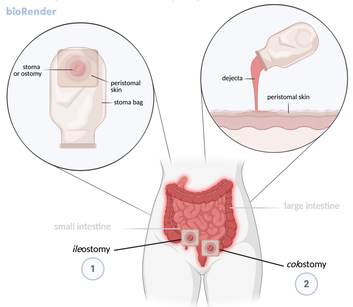
Julie V. Gawenda[1], Mirella A. Ejiugwo[1], Abram D. Janis[2], Shane Browne[1,3]

1. Tissue Engineering Research Group, Department of Anatomy and Regenerative Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland. 2. Hollister Incorporated, Libertyville, Illinois, United States. 3. CÙRAM, Centre for Research in Medical Devices, University of Galway, Galway, Ireland.

Background

An **ostomy** or **stoma**, a surgically created connection between a hollow organ and the body surface, is commonly performed to manage gastrointestinal disorders and injuries, with approximately 130,000 cases annually in the United States [1]. Despite its life-saving role, ostomies may have many complications, the most prevalent being **peristomal skin complications** (PSCs). PSCs arise primarily from the leakage of waste material (**dejecta**) onto the skin surrounding the stoma (**peristomal skin**) [2, 3]. However, factors contributing to PSC formation remain poorly understood.

Figure 1. The major gastrointestinal ostomies. *(1) An ileostomy, or diversion of the small intestine and (2) a colostomy, or diversion of the large intestine. An ostomy bag is fitted over the stoma.*



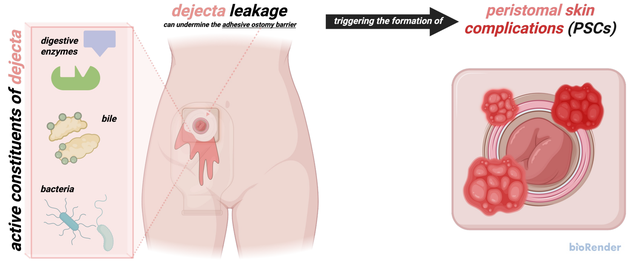


Figure 2. Dejecta leakage as a risk factor for PSCs. *Leakage can undermine the adhesive ostomy barrier, introducing the active constituents (digestive enzymes, bile, and bacteria) to the skin, triggering the formation of PSCs [2].*

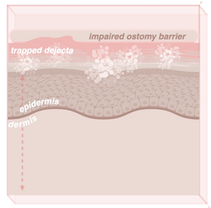
Methodology

This study systematically reviews the composition of dejecta, identifying active constituents (digestive enzymes, bile, and bacteria) and their potential impact on skin integrity. Furthermore, it evaluates relevant *in vitro* and *in vivo* models to investigate the pathogenesis of PSCs, and to help identify and test preventative or therapeutic approaches.

Databases: PubMed, Scopus, and Web of Science.
Keywords: "peristomal skin complications", "ileostomy", "dejecta", "ileostomy output", "bile", "digestive enzymes", "gut bacteria", "skin integrity", "*in vivo* model", "*in vitro* model".
Number of articles: 128 articles were identified and reviewed.

Results

Dejecta contains a complex mixture of components that can compromise the skin barrier if exposed to the peristomal skin, leading to PSCs. Initial findings suggest that **digestive enzymes**, **bile**, and **bacteria** play distinct roles.



DEJECTA CONSTITUENTS	FUNCTION WITHIN THE GI TRACT	POTENTIAL EFFECTS ON PERISTOMAL SKIN
DIGESTIVE ENZYMES	Assist with digestion of ingested food for nutrient absorption.	❑ Pancreatic lipase: Breaks down sebum and intercellular lipid lamellae within the stratum corneum. ❑ Chymotrypsin & trypsin: Cleave collagen, cause excessive desquamation, and increase transdermal penetration of macromolecules. ❑ Elastase: Cleaves elastin fibres.
BILE	Involved in dietary fat emulsification and breakdown for improved digestion and absorption. Reabsorbed along the terminal ileum.	❑ Bile acids (BAs) act as transdermal-enhancing excipients in drug formulation. ❑ BA exposure may increase skin permeability to digestive enzymes and bacteria.
BACTERIA	Contribute to carbohydrate and fat digestion, bile acid physiology, and micronutrient synthesis and absorption.	❑ Extracellular matrix (ECM) breakdown via collagenase production, with high activity from aerobes and facultative anaerobes. ❑ Microbial-induced synthesis of matrix metalloproteinases (MMPs), contributing to tissue degradation.

Table 1. The active constituents of dejecta*. The identified constituents of dejecta are introduced to the peristomal skin through dejecta leakage, impacting the epidermis and dermis, with potential effects on peristomal skin health summarized.*

CATEGORIZATION		SKIN MODEL	DISEASES MODELLED	ADVANTAGES	DISADVANTAGES
IN VIVO		Murine	Incontinence-associated dermatitis (IAD), peristomal dermatitis, psoriasis	1. Cost-effective purchase & maintenance 2. Fast reproductive cycle	1. Different body mass, GI tract length & wound-healing mechanisms 2. Void of mucosal folds and submucosa
		Porcine	Superantigen-induced dermatitis, IAD, allergic contact dermatitis, atopic dermatitis, psoriasis	1. Physiologically relevant (small intestine lumen and skin)	1. Contains overabundance of apocrine sweat glands 2. Expensive purchase & maintenance 3. Long reproductive wait-time
IN VITRO	**2D**	Monolayer	Psoriasiform cutaneous inflammation	1. Simple 2. Cost-effective 3. Easily reproducible	1. Involves singular cell type 2. Propagated on flat environment
		Co-culture	Atopic dermatitis	1. Simple 2. Cost-effective 3. Easily determine interactions between ≥ 2 cell types	1. Propagated on flat environment 2. Cells mixed with no layered differentiation
	3D	De-epidermized dermis (DED)	Parakeratosis, psoriasis	1. Physiologically relevant 2. Can culture for up to 4-5 weeks 3. Retains basement membrane antigens	1. Lacks viable fibroblasts 2. ECM cannot self-renew 3. Requires excessive skin biopsies
		Biomaterial-based	Psoriasis, eczematous dermatitis, diabetes	1. Increased customizability 2. Controlled & replicable biophysical properties	1. Limited shelf-life 2. Poor mechanical properties 3. Animal collagen not representative of human
		Self-assembly	Psoriasis, atopic dermatitis	1. No need for exogenous material or skin biopsies	1. Requires meticulous control over factors like pH, temperature, timing, and concentrations
	2D/3D	Skin-on-a-chip (SOC)	Atopic dermatitis, oedema	1. Combines aspects of 2D & 3D models (lateral flow, multilayer depth) 2. Controlled microenvironment	1. Generation and upkeep can be time-consuming 2. Requires microfabrication expertise

Table 2. Potential models for PSC characterisation. *Summary of the in vivo and in vitro diseased skin models of relevance to PSCs, describing the current disease model applications, advantages, and disadvantages of each approach.*

Conclusions and Future Directions

Understanding the interaction between active dejecta constituents and peristomal skin is critical to advance our knowledge of PSC pathogenesis.

- ❑ Existing stoma care research focuses on *preventative* solutions to dejecta leakage, such as flange stabilizers and ostomy bag sensors.
- ❑ Active constituents of dejecta such as digestive enzymes, bile, and bacteria contribute significantly to skin barrier disruption.
- ❑ The development of advanced *in vitro* models presents a promising and high-throughput approach to study PSCs without utilizing live subjects.
- ❑ An ostomate-specific *in vitro* model could account for comorbidities, for example, induce dermatitis via a cytokine cocktail, before triggering a PSC, and testing ostomy products like skin barriers.

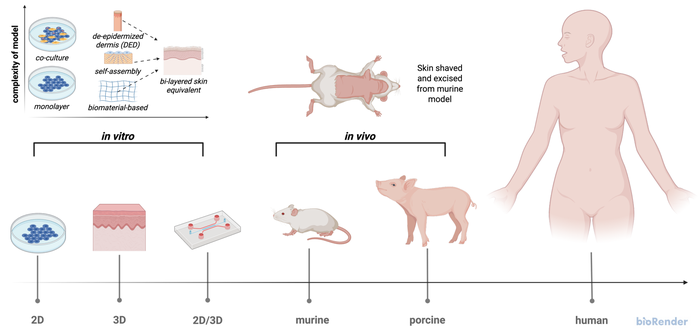


Figure 3. *A graphical summary depicting in vitro and in vivo models that could be used to study PSCs and PSC-like skin disorders, ranging from 2D (co-culture, monolayer) to 3D (DED, self-assembly, biomaterial-based) to human volunteers.*

References

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Full list of references (128) utilized in review can be accessed here: shorturl.at/DHpuh

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