COLOSTRUM FOR COSMETIC PURPOSE AND CELL REGENERATION

HEALTH TECHNOLOGY ASSESSMENT SECTION
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DISCLAIMER

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DISCLOSURE

The author of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia.

EXECUTIVE SUMMARY

Introduction

Bovine colostrum (BC) is the milk secreted by cows during the first few days after parturition. It contains many essential nutrients and bioactive components, including growth factors, immunoglobulins (Igs), lactoperoxidase (Lp), lysozyme (Lys), lactoferrin (Lf), cytokines, nucleosides, vitamins, peptides and oligosaccharides, which are of increasing relevance to human health. Human colostrum typically contains 2% IgG content, while bovine colostrum can have from 8% to above 25% IgG.

It is commercially regarded as a nutraceutical product and its claim to have numerous health benefits such as for treating viral and bacterial infections, gastrointestinal disorders, respiratory tract disorders and enhancing exercise performance in athlete.

This technology review was conducted following a request from National Pharmaceutical Control Bureau, Ministry of Health (MOH) Malaysia who received a proposal from a company to promote for licensing to market the product in cosmetic.

Objective/aim

To assess the safety, efficacy/effectiveness and cost-effectiveness of colostrum for cosmetic purpose and cell regeneration.

Results and conclusions

There was no retrievable scientific evidence on the safety, efficacy/effectiveness and cost-effectiveness of colostrum for cosmetic purpose and cell regeneration.

Methods

Electronic databases were searched through the MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, EBM Reviews - Cochrane Central Register of Controlled Trials -July 2013 and EBM Reviews - Health Technology Assessment - 3rd Quarter 2013, EBM Reviews-Database of Abstracts of Review of Effects-3rd Quarter 2013, EBM Reviews-Cochrane database of Systematic Reviews – 2005 until July 2013. Other database was PubMed, National Horizon Scanning and FDA website. Besides that, additional articles from bibliographies of retrieved articles and requestor lists were also included. There was no limit in the search. Relevant articles were critically appraised using Critical Appraisal Skills Programme (CASP) and the studies were graded according to US/Canadian Preventive Services Task Force (Harris 2001).

1. INTRODUCTION

Colostrum is the thin yellowish milk produced by the mammary glands of all mammals including humans during the first 72 hour after birth. It is fed to their newborns to provide essential nutrients and bioactive components including growth factors, immunoglobulins, vitamins, minerals and amino acids. It is rich in immunoglobulin which contain certain types of protein involved in promoting immune system.[1]

The resurgence of breastfeeding in the 1970s sparked a revival of interest in colostrum for both infants and adults. However, most commercial colostrum preparations come from cows, not humans. It is molecularly identical to human colostrum and is regarded highly by those using it for health benefits.

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Colostrum from the non immunized cows contains antibodies against enteric pathogens but the titre of the antibodies is too low to provide prophylaxis against infections has provoked interest in the development of immune milk preparation for microbial infection. This limitation has been overcome by using antibodies in hyperimmunize bovine colostrum (HBC) after vaccination of pregnant cow. The ability to direct the cow's immune system to produce antigen-specific antibodies may be used to provide preventions against specific pathogen continues to be an area of interest.[3]

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2. OBJECTIVE/AIM

To assess the safety, efficacy/effectiveness and cost-effectiveness of colostrum for cosmetic purpose and cell regeneration.

3. TECHNICAL FEATURES

3.1 Definition

3.1.1 Bovine Colostrum

BC is defined as the milk collected during the first “several days” postparturition. “Several days” has no definable standard however; it is generally considered that milk collected more than four days after calving is no longer considered BC.[4]

3.1.2 Hyperimmune Bovine Colostrum (HBC)

HBC is harvested during the first days after calving from cows that have been inoculated repeatedly with specific pathogens during pregnancy. High antibodies titre in the blood and colostrum can be achieved using the combination of intramuscular and inoculation at the end of the lactation period and during the dry period. In addition to high titres of anti-pathogen specific antibodies, HBC is also rich in other immune factors such as proline-rich polypeptides (PRP), lactoferrin, glycoproteins, lactalbumins, cytokines, growth factors, vitamins, and minerals. [5]

3.2 Colostrum Harvesting and Processing

BC does not have typical composition profile like some dietary supplements whose component is precisely defined chemically. Several factors may affect the composition of bovine colostrum including the breed, feeding practice and time collection post-parturition.

3.2.1 Harvesting

Calf health and productivity depends on colostrum quality and the acquisition of passive immunity. The calf is kept under close supervision in good state of hygiene and without exposure to antibiotic, pesticides and antihelmintics.

They also must receive colostrum, which contains the immunoglobulin called IgG to establish immune protection from disease. Calves must be fed approximately 100g of Immunoglobulin IgG before twelve hours of age and up to 200g of IgG by the time of gut closure at 24 hours of age. This means that dairy calves should receive 2-3 liters of good quality of colostrum for each two feedings, before the calf reaches 12 hours of age, and it must be fed as soon as possible after birth. After the calf receives all the IgG it needs for passive immunity and protection, the balance is collected and manufactured into powder. As dairy cows usually produce up to 22-24 liters of colostrum, there is still a large volume that can be collected and processed.[5]

It was recommended that BC should be harvested within 6 hours of parturition to obtain a high quality product. Immunoglobulin (Ig) concentrations in mammary secretions decrease with time after parturition. For example the product of BC that collected at 24 hours post-parturition would be expected to have a higher concentration of immunoglobulin (Ig) and growth factors than collected from the same cow after 3 days post-parturition.[7]

Colostrum and the main component of IgG are expressed as follows in the 60 hours following calving:

Table 1: This shows the rapid decrease of IgG within the first 60 hours period. This is the reason why only the first five milkings are collected.

Hours after Calving	IgG (mg/ml)
0	103
12	59
24	24
36	14
48	8
60	5

3.2.2 Pasteurisation (Low Temperature Processing)

Pasteurisation is necessary and is performed as to ensure microbiological quality. Typically this is performed at 72^0C for a period of 15 seconds. This process is done by specialized method to maintain the integrity of the biologically-active component and to destroy bacteria that may be present.[4]

3.2.3 Drying process

This carefully controlled procedure turns the liquid colostrum into a fine powder that is stable for prolonged periods. It is most commonly dehydrated by either spraying drying or freeze-drying.

3.3 Composition of Bovine Colostrum

The most important components of bovine colostrum can be broken down into three major categories: immune system factors, growth factors and metabolic factors.

3.3.1 Immune system Factors

Immunoglobulins - Also called antibodies, are proteins produced by the immune system in response to bacterial, virus or other foreign invasion. Immunoglobulins make up over 50% of the protein component, providing specific

anti-microbial protection by neutralizing bacteria, bacterial toxins, viruses and some parasites.

There are five types of immunoglobulins present in colostrum, specifically **IgA, IgD, IgE, IgG, & IgM**. Bovine colostrum contains mostly IgG with very small amounts of IgA, IgD, IgE, and IgM. In addition to immunoglobulins there are other immune factors present in milk and colostrum: including lactoferrin, transferrin, secretory component, lysozyme, oligosaccharides, glycolipids, and various hormones.

Table 2: Biological factors in Bovine Colostrum and their function

Component	Functions
Lactoferrin	Iron-binding protein, anti-microbial, anti-inflammatory
Transferrin	Iron-binding protein, antioxidant, anti-microbial
Secretory Component	Prostaglandin inhibitor, anti-inflammatory, anti-microbial
Interleukins	Stimulators of the immune response - by promoting proliferation and maturation of activated T cells
Interferons	Antiviral, stimulators of immune response by modulating the activity of natural killer cells.
Lyzozyme	Anti-microbial - acts in conjunction with secretory IgA to neutralizeharmful bacteria
Oligosccharides	Anti-microbial, inhibit the ability of harmful bacteria adhering to mucousal surface
Glycolipids	Various anti-microbial and modulator functions
Lactoperoxidase	Anti-microbial

3.3.2 Growth Factors

Colostrum is a very complex mixture containing many substances that have yet to be fully appreciated. Among these substances there is a group of low molecular weight peptides collectively referred to as "growth factors". Growth factors are hormone-like peptides that either act alone or in conjunction with other substances to affect the growth (proliferation) and maturation of various cell types**.**

Growth factors and cytokines present in colostrum and their respective actions are as follows:

Table 3: Growth factors in Bovine Colostrum and their functions

Component	Functions
Insulin Growth Factor 1 & 2	Stimulates muscle and bone cell proliferation and development. Involved in the anti-aging process
Epidermal Growth Factor	Stimulates tissue repair & wound healing and maturation of the digestive tract.
Fibroblast Growth Factor	Stimulates muscle and bone cell proliferation and development
Platelet Derived Growth Factor	Stimulates the proliferation and development of a wide range of cell types
Transforming Growth Factor	Stimulates tissue repair & wound healing

3.3.3 Metabolic Factors

The metabolic factors in colostrum aid our utilization of carbohydrates and play a role in normalizing weight problems.

Table 4: Metabolic factors in Bovine Colostrum and their functions

Component	Functions
Leptin	A small hormone-like protein that can suppress appetite and lead to body weight reduction.
Insulin	A hormone required for the effective utilization of glucose (blood sugar) in the body.
Vitamin-binding proteins	Smaller proteins that act as carriers to deliver B-complex vitamins to the body.
Fat-associated vitamins	Significant quantities of vitamins A, D, E and K are dissolved in or associated with the fat in colostrum.
Mineral-binding proteins	In addition to interfering with the replication of certain microorganisms, the iron-binding proteins, lactoferrin and transferrin, also serve to capture iron from ingested sources and present it in a form that can be readily absorbed by the body
Cyclic adenosine monophosphate (cAMP)	A phosphorylated nucleotide in a very specialized form that transfers the chemical energy necessary to drive metabolic reactions to form new protein, carbohydrate and fat molecules.
Enzyme inhibitors	These small proteins slow down or inhibit the breakdown of proteins by certain enzymes.

4. METHODS

4.1 Searching

Literature search was done to search for published articles on the safety, efficacy/effectiveness and cost-effectiveness of colostrum.

Electronic databases were searched through the Ovid interface:

- MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to present
- EBM Reviews - Cochrane Central Register of Controlled Trials- July 2013
- EBM Reviews – Database of Abstracts of Review of Effects (3rd Quarter 2013)
- EBM Reviews - Cochrane Database of Systematic Reviews – (2005 until July 2013)
- EBM Reviews - Health Technology Assessment – 3rd Quarter 2013
- NHS economic evaluation database – 3rd Quarter 2013

Other databases;

- PubMed
- Horizon Scanning database (National Horizon Scanning Centre)
- USFDA website

No limits were applied to the search. Detailed search strategy is as in **Appendix 1.** In addition, other search engine such as Google was used to search for additional web based-materials and information. Additional articles such as from reviewing the references of retrieved articles were also included.

The last search was conducted on 2nd September 2013

4.2 Selection

Based on the inclusion and exclusion criteria, study selection were carried out. The titles and abstracts of all studies were assessed for the eligibility criteria. The inclusion and exclusion criteria as stated below:

Inclusion criteria

Population	General population Women
Interventions	Bovine Colostrum, Hyperimmune Bovine Colostrum
Comparators	Whey protein, placebo
Outcomes	Cosmetic Enhance cell regeneration Anti-ageing
Study design	Systematic review, Randomized Controlled Trial (RCT), Health Technology Assessment (HTA), Cohort and Case Control study

Exclusion criteria

Study design	Case series, case report, survey, anecdotal, animal studies
Publication	Non English full text articles

Relevant articles were critically appraised using Critical Appraisal Skills Programme (CASP) and evidence graded according to the US / Canadian Preventive Services Task Force. **(Appendix 2)**

5. RESULTS AND DISCUSSION

There was no retrievable scientific evidence on the safety, efficacy/effectiveness and cost-effectiveness of colostrum for cosmetic purpose and cell regeneration from journal databases. Under USFDA regulations colostrum can be generally recognized as safe (GRAS) as it complies with the Dietary Supplement Current Good Manufacturing Practices (CGMPs).

5.2 Limitation

Our review has several limitations. The selection of the studies and appraisal was done by one reviewer. Although there was no restriction in language during the search, only English full text articles were included in the report.

6.0 CONCLUSION

There was no retrievable scientific evidence on the safety and efficacy/ effectiveness and cost-effectiveness of colostrum for cosmetic purpose and cell regeneration from electronic databases.

7. REFERENCES

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8. APPENDIX

8.1. Appendix 1: LITERATURE SEARCH STRATEGY

Ovid MEDLINE® In-process & other Non-Indexed citations and OvidMEDLINE® 1948 to present

1. Colostrum/
2. colostrum$.tw.
3. (bovine adj1 colostrum$).tw.
4. (hyperimmune adj1 bovine colostrum).tw.
5. (bovine adj1 immunoglobulin).tw.
6. 1 or 2 or 3 or 4 or 5
7. Milk Proteins/
8. (milk adj1 protein$).tw.
9. whey protein.tw.
10. 7 or 8 or 9
11. Anti-ageing.tw.
12. Cell regeneration.tw.
13. 11 or 12
14. 6 or 10 and 13

OTHER DATABASES

EBM Reviews - Cochrane Central Register of Controlled Trials	Same MeSH, keywords, limits used as per MEDLINE search
EBM Reviews - Database of Abstracts of Review of Effects	
EBM Reviews - Cochrane database of systematic reviews	
EBM Reviews - Health Technology Assessment	
PubMed	
NHS economic evaluation database	
FDA	Colostrum

8.2. Appendix 2

HIERARCHY OF EVIDENCE FOR EFFECTIVENESS STUDIES

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)